PREPARATION AND USE OF SUPERIOR VACCINES

TECHNICAL FIELD

The present invention is directed to enhanced immunotherapy of human malignancies such as cancers.

BACKGROUND

The complex relationships between the immune system and tumor cells during the course of their pathogenesis have not been thoroughly understood. However, the mere fact that a host immune system has the potential to recognize and eventuallv eradicate tumor cells has warranted immunotherapy as one of the most promising approaches for cancer treatment. Most tumors express altered or abnormal gene products as the result of uncontrolled cell growth and malignant transformation. These abnormal gene products are often antigenic to the host immune system, rendering the tumor cells potentially susceptible to immunocytolysis. Gilboa et al. (1998) Cancer Imm. Immunother. 46:82-87.

Cytotoxic T lymphocyte (CTL)-mediated cellular immunity is regarded as an important weapon for a host defense system against many tumors. A variety of molecular factors determine whether a tumor cell can be recognized by the host immune system and eventually lysed by CTL. Lindauer et al. (1998) J. Mol. Med. 76:32-47. Tumor associated antigens are proteolytically degraded into small peptide epitopes that compete for binding to and presentation by a finite number of major histocompatibility complex (MHC) molecules. The formed MHC-peptide complexes can be recognized by naïve CTLs via their T cell receptors. Further activation of the naïve CTLs requires functions of costimulatory factors, most of which are associated with professional antigen presenting cells (APCs). The activated antigen-specific CTLs then differentiate into cytolytic effector cells that are capable of lysing tumor cells bearing specific tumor antigens.

Various tumor associated antigens have been identified so far, with the vast majority being melonoma-related. Lindauer et al. supra. Tumor associated antigens can be categorized into four classes: the differentiation antigens which are normal proteins over-expressed by tumor cells such as gp100; viral antigens such as HPV16 E6 and E7; the cancer/testes family of antigens typified by MAGE; and the mutated proteins such as ras or p53. All these tumor antigens, when processed properly and presented favorably by MHC molecules, can be the targets for recognition and binding by T cell receptors.

However, mere presentation of the tumor antigen via MHC and subsequent recognition by T cell receptors are not insufficient to activate a robust cytotoxic immune response that can lyse the tumor cells. Many co- factors having immunostimulatory functions are necessary for efficient CTL activation. Indeed, binding and stimulating T cell receptors in the absence of these costimulatory factors may cause the T cells to be unresponsive to further antigenic stimulation, which is an anergy state potentially responsible for immune tolerance to many tumor self antigens.

Costimulatory functions have primarily been associated with professional antigen-presenting cells (APC). For example, upon exposure to specific signals such as inflammatory agents, APCs have the capacity to up-regulate T cell proliferation and IL-2 production, which are necessary processes for CTL activation. APCs are also known for secreting T cell growth factors to amplify antigen-specific CTL response. In addition, activated APCs can provide a favorable lymphoid environment for antigen presentation and CTL activation, either by secreting chemokines that can induce the migration of immune effector cells to antigen presenting sites; or by migrating to T cell rich sites such as draining lymph nodes where favorable APC:T cell interactions can occur.

Various gene based vaccines have been used to deliver transgenes encoding tumor antigen to APCs in vivo for antigen presentation, but very few are proven effective to elicite anti-tumor immunoactivity. While these gene based vaccines, including genetically modified APCs, may be efficient for antigen

presentation, they do not provide any modulation of the functional state of the endogenous APCs such as stimulating/facilitating the activation of T-cells. The present invention addresses this limitation and provides an enhanced vaccine composition for eliciting effective anti-tumor immune responses.

DISCLOSURE OF THE INVENTION

This invention provides an isolated population of polynucleotides comprising or corresponding to at least one polynucleotide shown in Table 1 and their respective complements. It also provides a polynucleotide encoding a ligand or antibody or engineered protein that binds to a cell surface protein of an antigen presenting cell and wherein the polynucleotide comprises or corresponds to a polynucleotide shown in Table 1 or its complement. The invention further provides a polynucleotide that encodes a transcription factor and wherein the polynucleotide comprises or corresponds to a polynucleotide shown in Table 1 or its complement.

Further provided herein is a polynucleotide comprising a first polynucleotide comprising encoding an immunostimulatory factor that is differentially expressed in an antigen presenting cell and comprising or corresponding to a tag shown in Table 1 or its complement. In one embodiment, the first polynucleotide encodes a factor selected from the group consisting of PARC, TARC, monocyte chemoattractant protein-4 (MDP-4), MDC, escalectin, MCP-2 or a biologically active fragments thereof. The polynucleotides can further comprise a first and second promoter, wherein the first and second polynucleotides are under the transcriptional control of the first and second promoters, respectively.

Also provided by this invention is a polynucleotide comprising a first polynucleotide comprising encoding an immunostimulatory factor that is differentially expressed in an antigen presenting cell that is differentially expressed in an antigen presenting cell and comprising or corresponding to a tag shown in Table 1 and second polynucleotide that modulates the expression of the

first polynucleotide. Further provided is a polynucleotide comprising a first polynucleotide encoding an antigen and a second polynucleotide that modulates the expression of a third polynucleotide which encodes an immunstimulatory factor that is differentially expressed in an antigen presenting cell, wherein the third polynucleotide comprises or corresponds to a tag shown in Table 1. The first polynucleotide may encode PARC, monocyte chemoattractant protein-4 (MDP-4), MDC, escalectin, MCP-2 or a biologically active fragments thereof. Also provided herein is a polynucleotide comprising a first polynucleotide encoding an engineered protein or polypeptide that binds to a cell surface protein of antigen presenting cells thereby modulating either directly or indirectly by a signal transduction pathway and a second polynucleotide encoding an immunostimulatory factor comprising or corresponding to a tag shown in Table 1. Promoters can be operatively linked to the polynucleotides to direct expression thereof.

The polynucleotides can be inserted within a gene delivery vehicle or a host cell. Alternatively they can be attached to a chip or within a database for computational analysis.

The compositions of this invention are useful to induce an immune response in a subject. They also are useful to modulate the genotype of an antigen presenting and to screen for a candidate therapeutic agent that modulates the expression of a polynucleotide differentially expressed in an antigen.

BRIEF DESCRIPTION OF THE TABLE

The Table depicts a series of mRNA sequences, identified by SAGE analysis. Tags isolated from various populations were isolated and analyzed: tags expressed in monocytes; tags expressed in monocyte-derived immature dendritic cells; and tags expressed in monocyte-derived mature dendritic cells, that have been stimulated to mature with TNFα. The columns of the tables are as follows: "Accession" is the accession number for the EST in the public databases; "tag" is the 10mer SAGE tag; "Seq. ID No." is the corresponding Sequence ID number

for the tag found at the end of the specification and claims. The description identifies the known gene or EST that corresponds to a tag. If the description section is blank or contains "NM" that identifies a novel tag as no match was found.

MODE(S) FOR CARRYING OUT THE INVENTION

Throughout this disclosure, various publications, patents and published patent specifications are referenced by an identifying citation. The disclosures of these publications, patents and published patent specifications are hereby incorporated by reference into the present disclosure to more fully describe the state of the art to which this invention pertains.

The practice of the present invention employs, unless otherwise indicated, conventional techniques of molecular biology (including recombinant techniques), microbiology, cell biology, biochemistry and immunology, which are within the skill of the art. Such techniques are explained fully in the literature. These methods are described in the following publications. See, e.g. Sambrook et al. MOLECULAR CLONING: A LABORATORY MANUAL, 2nd edition (1989); CURRENT PROTOCOLS IN MOLECULAR BIOLOGY (F. M. Ausubel et al. eds. (1987)); the series METHODS IN ENZYMOLOGY (Academic Press, Inc.); "PCR: A PRACTICAL APPROACH" (M. MacPherson et al. IRL Press at Oxford University Press (1991)); PCR 2: A PRACTICAL APPROACH (M.J. MacPherson. B.D. Hames and G.R. Taylor eds. (1995)); ANTIBODIES, A LABORATORY MANUAL (Harlow and Lane eds. (1988)); and ANIMAL CELL CULTURE (R.I. Freshney ed. (1987)).

As used herein, certain terms may have the following defined meanings.

The singular form "a", "an" and "the" include plural references unless the context clearly dictates otherwise. For example, the term "a cell" includes a plurality of cells, including mixtures thereof.

The term "comprising" is intended to mean that the compositions and methods include the recited elements, but not excluding others. "Consisting essentially of" when used to define compositions and methods, shall mean excluding other elements of any essential significance to the combination. Thus, a

composition consisting essentially of the elements as defined herein would not exclude trace contaminants from the isolation and purification method and pharmaceutically acceptable carriers, such as phosphate buffered saline. preservatives, and the like. "Consisting of" shall mean excluding more than trace elements of other ingredients and substantial method steps for administering the compositions of this invention. Embodiments defined by each of these transition terms are within the scope of this invention.

The terms "polynucleotide" and "nucleic acid molecule" are used interchangeably to refer to polymeric forms of nucleotides of any length. The polynucleotides may contain deoxyribonucleotides, ribonucleotides, and/or their analogs. Nucleotides may have any three-dimensional structure, and may perform any function, known or unknown. The term "polynucleotide" includes, for example, single-, double-stranded and triple helical molecules, a gene or gene fragment, exons, introns, mRNA, tRNA, rRNA, ribozyn es, cDNA, recombinant polynucleotides, branched polynucleotides, plasmids, vectors, isolated DNA of any sequence, isolated RNA of any sequence, nucleic acid probes, and primers. A nucleic acid molecule may also comprise modified nucleic acid molecules.

A "gene" refers to a polynuclec tide containing at least one open reading frame that is capable of encoding a particular polypeptide or protein after being transcribed and translated.

A "gene product" refers to the amino acid (e.g. peptide or polypeptide) generated when a gene is transcribed and translated.

As used herein a second polynucleotide "corresponds to" another (a first) polynucleotide if it is related to the first polynucleotide by any of the following relationships:

1) The second polynucleotide comprises the first polynucleotide and the second polynucleotide encodes a gene product.

2) The second polynucleotide is 5' or 3' to the first polynucleotide in cDNA, RNA, genomic DNA, or fragment of any of these polynucleotides. For example, a second polynucleotide may be a fragment of a gene that includes the

first and second polynucleotides. The first and second polynucleotides are related in that they are components of the gene coding for a gene product, such as a protein or antibody. However, it is not necessary that the second polynucleotide comprises or overlaps with the first polynucleotide to be encompassed within the definition of "corresponding to" as used herein. For example. the first polynucleotide may be a fragment of a 3' untranslated region of the second polynucleotide, e.g., it may comprise a promoter sequence for the gene comprising the tag. The first and second polynucleotide may be fragment of a gene coding for a gene product. The second polynucleotide may be an exon of the gene while the first polynucleotide may be an intron of the gene.

3) The second polynucleotide is the complement of the first polynucleotide.

A "foreign polynucleotide" is a DNA sequence that is foreign to the cell, vector or position therein, wherein it is placed.

A "sequence tag" or "tag" or "SAGE tag" is a short oligonucleotide containing defined nucleotide sequence that occurs in a certain position of a gene transcript. The length of a tag is generally under about 20 nucleotides, preferably between 9 to 15 nucleotides, and more preferably 10 nucleotides. The tag can be used to identify the corresponding transcript and gene from which it was transcribed. A tag can further comprise exogenous nucleotide sequences to facilitate the identification and utility of the tag. Such auxiliary sequences include, but are not limited to, restriction endonuclease cleavage sites and well known primer sequences for sequencing and cloning.

The term "peptide" is used in its broadest sense to refer to a compound of two or more subunit amino acids, amino acid analogs, or peptidomimetics. The subunits may be linked by peptide bonds. In another embodiment, the subunit may be linked by other bonds, e.g. ester, ether, etc. As used herein the term "amino acid" refers to either natural and/or unnatural or synthetic amino acids, including glycine and both the D or L optical isomers, and amino acid analogs and peptidomimetics. A peptide of three or more amino acids is commonly called

an oligopeptide if the peptide chain is short. If the peptide chain is long, the peptide is commonly called a polypeptide or a protein.

The term "cDNAs" refers to complementary DNA, that is mRNA molecules present in a cell or organism made in to cDNA with an enzyme such as reverse transcriptase. A "cDNA library" is a collection of all of the mRNA molecules present in a cell or organism, all turned into cDNA molecules with the enzyme reverse transcriptase, then inserted into "vectors".

A "probe" when used in the context of polynucleotide manipulation refers to an oligonucleotide that is provided as a reagent to detect a target potentially present in a sample of interest by hybridizing with the target. Usually, a probe will comprise a label or a means by which a label can be attached, either before or subsequent to the hybridization reaction. Suitable labels include, but are not limited to radioisotopes, fluorochromes, chemiluminescent compounds, dyes, and proteins, including enzymes.

A "primer" is a short polynucleotide, generally with a free 3' -OH group that binds to a target or "template" potentially present in a sample of interest by hybridizing with the target, and thereafter promoting polymerization of a polynucleotide complementary to the target. A "polymerase chain reaction" ("PCR") is a reaction in which replicate copies are made of a target polynucleotide using a "pair of primers" or a "set of primers" consisting of an "upstream" and a "downstream" primer, and a catalyst of polymerization, such as a DNA polymerase, and typically a thermally-stable polymerase enzyme. Methods for PCR are well known in the art, and taught, for example in "PCR: A PRACTICAL APPROACH" (M. MacPherson *et al.*, IRL Press at Oxford University Press (1991)). All processes of producing replicate copies of a polynucleotide, such as PCR or gene cloning, are collectively referred to herein as "replication." A primer can also be used as a probe in hybridization reactions, such as Southern or Northern blot analyses. Sambrook et al., *supra.*

A "promoter" is a region on a DNA molecule to which an RNA polymerase binds and initiates transcription. In an operon, the promoter is usually

located at the operator end, adjacent but external to the operator. The nucleotide sequence of the promoter determines both the nature of the enzyme that attaches to it and the rate of RNA synthesis.

The term "genetically modified" means containing and/or expressing a foreign gene or nucleic acid sequence which in turn, modifies the genotype or phenotype of the cell or its progeny.

As used herein, "expression" or "expressed" refers to the process by which polynucleotides are transcribed into mRNA or by which transcription is enhanced. In another embodiment, the RNA is translated into peptides, polypeptides, or proteins. If the polynucleotide is derived from genomic DNA, expression may include splicing of the mRNA, if an appropriate eukaryotic host is selected.

"Differentially expressed" as applied to a gene, refers to the differential production of the mRNA transcribed from the gene or the protein product encoded by the gene. A differentially expressed gene may be overexpressed or underexpressed as compared to the expression level of a normal or control cell. In one aspect, it refers to a differential that is 3 times, preferably 5 times, or preferably 10 times higher or lower than the expression level detected in a control sample. The term "differentially expressed" also refers to nucleotide sequences in a cell or tissue which are expressed where silent in a control cell or not expressed where expressed in a control cell.

A "native" or "natural" antigen is a polypeptide, protein or a fragment which contains an epitope, which has been isolated from a natural biological source, and which can specifically bind to an antigen receptor, in particular a T cell antigen receptor (TCR), in a subject. It also substances which are immunogenic, i.e., immunogens, as well as substances which induce immunological unresponsiveness, or anergy, i.e., anergens.

A "self-antigen" also referred to herein as a native or wild-type antigen is an antigenic peptide that induces little or no immune response in the subject due

to self- tolerance to the antigen. An example of a self-antigen is the human melanoma antigen gp 100.

The term "tumor associated antigen" or "TAA" refers to an antigen that is associated with or specific to a tumor. Examples of known TAAs include gp100, MART and MAGE.

The term "lysing" refers to the action of rupturing the cell wall and/or cell membrane of a cell through cytotoxic T-cell lymphocyte (CTL)-mediated cellular immunity. In a preferred embodiment, the lysis of cells is done to release cellular constituents from the lysed cells. For purposes of the present invention. "cellular constituents" is meant any component found within a cell. Such components include, but are not limited to, proteins, lipoproteins, glycoproteins, lipids. carbohydrates, nucleic acids, steroids, prostaglandins, and combinations and complexes thereof. The components are also referred to as "endogenous antigens."

A "gene delivery vehicle" is defined as any molecule that can carry inserted polynucleotides into a host cell. Examples of gene delivery vehicles are liposomes, viruses, such as baculovirus, adenovirus and retrovirus, bacteriophage, cosmid, plasmid, fungal vectors and other recombination vehicles typically used in the art which have been described for expression in a variety of eukaryotic and prokaryotic hosts, and may be used for gene therapy as well as for simple protein expression.

A "viral vector" is defined as a recombinantly produced virus or viral particle that comprises a polynucleotide to be delivered into a host cell, either *in vivo, ex vivo* or *in vitro*. Examples of viral vectors include retroviral vectors, adenovirus vectors, adeno-associated virus vectors and the like. In aspects where gene transfer is mediated by a retroviral vector, a vector construct refers to the polynucleotide comprising the retroviral genome or part thereof, and a therapeutic gene. As used herein, "retroviral mediated gene transfer" or "retroviral transduction" carries the same meaning and refers to the process by which a gene or nucleic acid sequences are stably transferred into the host cell by virtue of the

virus entering the cell and integrating its genome into the host cell genome. The virus can enter the host cell via its normal mechanism of infection or be modified such that it binds to a different host cell surface receptor or ligand to enter the cell. As used herein, retroviral vector refers to a viral particle capable of introducing exogenous nucleic acid into a cell through a viral or viral-like entry mechanism.

The term "isolated" means separated from constituents, cellular and otherwise, in which the polynucleotide, peptide, polypeptide, protein, antibody, or fragments thereof, are normally associated with in nature. In addition, a "concentrated", "separated" or "diluted" polynucleotide, peptide, polypeptide, protein, antibody, or fragments thereof, is distinguishable from its naturally occurring counterpart in that the concentration or number of molecules per volume is greater than "concentrated" or less than "separated" than that of its naturally occurring counterpart. Although not explicitly stated for each of the inventions disclosed herein, it is to be understood that all of the above embodiments for each of the compositions disclosed below and under the appropriate conditions, are provided by this invention. Thus, a non-naturally occurring polynucleotide is provided as a separate embodiment from the isolated naturally occurring polynucleotide. A protein produced in a bacterial cell is provided as a separate embodiment from the naturally occurring protein isolated from a eukaryotic cell in which it is produced in nature.

"Host cell" or "recipient cell" is intended to include any individual cell or cell culture which can be or have been recipients for vectors or the incorporation of exogenous nucleic acid molecules, polynucleotides and/or proteins. It also is intended to include progeny of a single cell, and the progeny may not necessarily be completely identical (in morphology or in genomic or total DNA complement) to the original parent cell due to natural, accidental, or deliberate mutation. The cells may be prokaryotic or eukaryotic, and include but are not limited to bacterial cells, yeast cells, animal cells, and mammalian cells, e.g., murine, rat, simian or human.

A "subject" is a vertebrate, preferably a mammal, more preferably a human. Mammals include, but are not limited to, murmes, simians, humans, farm animals, sport animals, and pets.

A "control" is an alternative subject or sample used in an experiment for comparison purpose. A control can be "positive" or "negative. " For example, where the purpose of the experiment is to determine a correlation of an altered expression level of a proto-oncogene with a particular type of cancer, it is generally preferable to use a positive control (a subject or a sample from a subject, carrying such alteration and exhibiting syndromes characteristic of that disease), and a negative control (a subject or a sample from a subject lacking the altered expression and clinical syndrome of that disease).

The terms "major histocompatibility complex" or "MHC" refers to a complex of genes encoding cell-surface molecules that are required for antigen presentation to T cells and for rapid graft rejection. The proteins encoded by the MHC complex are known as "MHC molecules" and are classified into class I and class II MHC molecules. Class I MHC molecules include membrane heterodimeric proteins made up of an a chain encoded in the MHC associated noncovalently with b2-microglobulin. Class I MHC molecules are expressed by nearly all nucleated cells and have been shown to function in antigen presentation to $CD8^+$ T cells. Class I molecules include HLA-A, -B, and -C in humans. Class II MHC molecules also include membrane heterodimeric proteins consisting of noncovalently associated a and b chains. Class II MHC are known to participate in antigen presentation to $CD4^+$ T cells and, in humans, include HLA-DP, -DQ, and DR. The term "MHC restriction"refers to a characteristic of T cells that permits them to reorganize antigen only after it is processed and the resulting antigenic peptides are displayed in association with either a self class I or class II MHC molecule. Methods of identifying and comparing MHC are well known in the art and are described in Allen, M. et al. (1994) Human Immunol. 40:25-32; Santamaria, P. et al. (1993) Human Immunol. 37:39-50 and Hurley, C.K. et al. (1997) Tissue Antigens 50:401-415.

The term "antigen presenting cells (APC)" refers to a class of cells capable of presenting one or more antigens in the form of antigen-MHC complex recognizable by specific effector cells of the immune system, and thereby inducing an effective cellular immune response against the antigen or antigens being presented. While many types of cells may be capable of presenting antigens on their cell surface for T-cell recognition, only professional APCs have the capacity to present antigens in an efficient amount and further to activate T-cells for cytotoxic T-lymphocyte (CTL) response. APCs can be intact whole cells such as macrophages, B-cells and dendritic cells; or other molecules, naturally occurring or synthetic, such as purified MHC class I molecules complexed to beta2-microglobulin.

The term "dendritic cells (DC)" refers to a diverse population of morphologically similar cell types found in a variety of lymphoid and non-lymphoid tissues (Steinman (1991) Ann. Rev. Immunol. 9:271-296). Dendritic cells constitute the most potent and preferred APCs in the organism. At least a subset, if not all, dendritic cells are derived from bone marrow progenitor cells, circulate in small numbers in the peripheral blood and appear either as immature Langerhans' cells or terminally differentiated mature cells. While the dendritic cells can be differentiated from monocytes, they possess distinct phenotypes. For example, a particular differentiating marker, CD14 antigen, is either absent or present at low levels in dendritic cells, but is possessed by monocytes. Also, dendritic cells are not phagocytic, whereas the monocytes are strongly phagocytosing cells. It has been shown that DCs provide all the signals necessary for T cell activation and proliferation.

"Co-stimulatory molecules" are involved in the interaction between receptor-ligand pairs expressed on the surface of antigen presenting cells and T cells. Research accumulated over the past several years has demonstrated convincingly that resting T cells require at least two signals for induction of cytokine gene expression and proliferation (Schwartz R.H. (1990) Science 248:1349-1356 and Jenkins M.K. (1992) Immunol. Today 13:69-73). One signal,

the one that confers specificity, can be produced by interaction of the TCR/CD3 complex with an appropriate MHC/peptide complex. The second signal is not antigen specific and is termed the "co-stimulatory" signal. This signal was originally defined as an activity provided by bone-marrow-derived accessory cells such as macrophages and dendritic cells, the so called "professional" APCs. Several molecules have been shown to enhance co-stimulatory activity. These are heat stable antigen (HSA) (Liu Y. et al. (1992) J. Exp. Med. 175:437-445); chondroitin sulfate-modified MHC invariant chain (ICS) (Naujokas M.F. et al. (1993) Cell 74:257-268); intracellular adhesion molecule 1 (ICAM-1) (Van Seventer G.A. (1990) J. Immunol. 144:4579-4586); and B7-1 and B7-2/B70 (Schwartz R.H. (1992) Cell 71:1065-1068). Co-stimulatory molecules are commercially available from a variety of sources, including, for example, Beckman Coulter. It is intended, although not always explicitly stated, that molecules having similar biological activity as wild-type or purified co-stimulatory molecules (*e.g.*, recombinantly produced or muteins thereof) are intended to be used within the spirit and scope of the invention.

As used herein, the term "cytokine" refers to any one of the numerous factors that exert a variety of effects on cells, for example, inducing growth or proliferation. Non-limiting examples of cytokines which may be used alone or in combination in the practice of the present invention include. interleukin-2 (IL-2), stem cell factor (SCF), interleukin 3 (IL-3), interleukin 6 (IL-6), interleukin 12 (IL-12), G-CSF, granulocyte macrophage-colony stimulating factor (GM-CSF), interleukin-1 alpha (IL-1), interleukin-11 (IL-11), MIP- 1, leukemia inhibitory factor (LIF), c-kit ligand, thrombopoietin (TPO) and flt3 ligand. The present invention also includes culture conditions in which one or more cytokine is specifically excluded from the medium. Cytokines are commercially available from several vendors such as, for example, Genentech (South San Francisco, CA), Amgen (Thousand Oaks, CA), R&D Systems (Minneapolis, MN) and Immunex (Seattle, WA). It is intended, although not always explicitly stated, that molecules having similar biological activity as wild-type or purified cytokines

(e.g., recombinantly produced or muteins thereof) are intended to be used within the spirit and scope of the invention.

The term "culturing" refers to the *in vitro* propagation of cells or organisms on or in media of various kinds. It is understood that the descendants of a cell grown in culture may not be completely identical (i.e., morphologically, genetically, or phenotypically) to the parent cell. By "expanded" is meant any proliferation or division of cells.

A "composition" is intended to mean a combination of active agent and another compound or composition, inert (for example, a detectable agent or label) or active. such as an adjuvant.

A "pharmaceutical composition" is intended to include the combination of an active agent with a carrier, inert or active, making the composition suitable for diagnostic or therapeutic use *in vitro, in vivo* or *ex vivo.*

An "effective amount" is an amount sufficient to effect beneficial or desired results. An effective amount can be administered in one or more administrations, applications or dosages.

The terms "cancer," "neoplasm," and "tumor," used interchangeably and in either the singular or plural form, refer to cells that have undergone a malignant transformation that makes them pathological to the host organism. Primary cancer cells (that is, cells obtained from near the site of malignant transformation) can be readily distinguished from non-cancerous cells by well-established techniques, particularly histological examination. The definition of a cancer cell, as used herein, includes not only a primary cancer cell, but any cell derived from a cancer cell ancestor. This includes metastasized cancer cells, and *in vitro* cultures and cell lines derived from cancer cells. When referring to a type of cancer that normally manifests as a solid tumor, a "clinically detectable" tumor is one that is detectable on the basis of tumor mass; *e.g.* by such procedures as CAT scan, magnetic resonance imaging (MRI), X-ray, ultrasound or palpation. Biochemical or immunologic findings alone may be insufficient to meet this definition. Tumor cells often express antigens which are tumor specific. The term "tumor associated

antigen" or "TAA" refers to an antigen that is associated with or specific to a tumor.

As used herein, "solid phase support" is not limited to a specific type of support. Rather a large number of supports are available and are known to one of ordinary skill in the art. Solid phase supports include silica gels, resins, derivatized plastic films, glass beads, cotton, plastic beads. alumina gels. A suitable solid phase support may be selected on the basis of desired end use and suitability for various synthetic protocols. For example, for peptide synthesis, solid phase support may refer to resins such as polystyrene (*e.g.*, PAM-resin obtained from Bachem Inc.. Peninsula Laboratories, etc.), POLYHIPE® resin (obtained from Aminotech, Canada), polyamide resin (obtained from Peninsula Laboratories), polystyrene resin grafted with polyethylene glycol (TentaGel®, Rapp Polymere, Tubingen, Germany) or polydimethylacrylamide resin (obtained from Milligen/Biosearch, California). In a preferred embodiment for peptide synthesis, solid phase support refers to polydimethylacrylamide resin.

A "transgenic animal" refers to a genetically engineered animal or offspring of genetically engineered animals. The transgenic animal may contain genetic material from at least one unrelated organism (such as from a bacteria, virus, plant, or other animal) or may contain a mutation which interferes with expression of a gene product.

The present invention provides enhanced anti-tumor vaccines in which a polypeptide or polypeptides encoding tumor antigens are linked to a polypeptide or polypeptides encoding immunostimulatory factors associated with APC functions. The co-administration of tumor antigens and APC-associated stimulatory factors will not only enable adequate antigen presentation to endogenous APCs but also enhance functions of the APCs for 1) presentation of co-stimulatory signals; 2) migration to T-cell rich sites; 3) secretion of T-cell growth factors; or 4) secretion of chemokines for recruitment of immune effector cells.

The immunostimulatory factors of this invention include any polypeptide factors that modulate immune responses mediated by APC and corresponding T cells. For example, co-stimulatory factors that are differentially expressed in APCs can be used directly to boost the APC functions in vivo. Co-stimulatory factors have been described above and include, but not limited to, heat stable antigen (HSA); chondroitin sulfate-modified MHC invariant chain (Ii-CS); intracellular adhesion molecule 1; and B7-1 and B7-2/B70. Also, the immunostimulatory factors of the invention can be gene regulatory factors that modulate the expression and activity of the above-described APC-associated co-stimulatory factors. In addition, ligands of APC-associated co-stimulatory factors can be used to create an autocrine loop whereby the genetically modified APC secrets a soluble ligand which is then available to bind cell surface receptors and activate the APC.

For the purpose of this invention, polypeptides and the polynucleotides encoding cell-specific antigens can be, in one embodiment, previously characterized tumor-associated antigens such as melanoma-associated antigen gp 100 (Kawakami et al. (1997) Intern. Rev. Immunol. 14:173-192); MUC-1 (Henderson et al. (1996) Cancer Res. 56:3763); MART-1 (Kawakami et al. (1994) Proc. Natl. Acad. Sci. 91:3515; Ribas et al. (1997) Cancer Res. 57:2865); HER-2/neu (U.S. Patent No. 5,550,214); MAGE (PCT/US92/04354); HPV16, 18E6 and E7 (Ressing et al. (1996) Cancer Res. 56(1):582; Restifo (1996) Current Opinion in Immunol. 8:658; Stern (1996) Adv. Cancer Res. 69:175; Tindle et al. (1995) Clin. Exp. Immunol. 101:265; van Driel et al. (1996) Annals of Medicine 28:471); CEA (U.S. Patent No. 5,274,087); PSA (Lundwall, A. (1989) Biochem. Biophys. Research Communications 161:1151); prostate specific membrane antigen (PSMA) (Israeli et al. (1993) Cancer Research 53:227); tyrosinase (U.S. Patent Nos. 5,530,096 and 4,898,814; Brichard et al. (1993) J. Exp. Med. 178:489); tyrosinase related proteins 1 or 2 (TRP-1 and TRP-2); NYESO-1 (Chen et al. (1997) Proc. Natl. Acad. Sci. U.S.A. 94:1914), or the GA733 antigen (U.S. Patent No. 5,185,254).

Selection of immunostimulatory factors of the invention

Embodiments of the present invention include immunostimulatory factors that are preferentially or differentially expressed in monocyte-derived dedritic cells. Many comparative gene expression analysis can be used to identify genes and mRNAs preferentially or differentially expressed in monocyte-derived dedritic cells as compared to other cells such as the monocyte precursor cells. One preferred method is the SAGE analysis--Serial Analysis of Gene Expression (Velculescu, et al. (1995) Science 270:484-487 and U.S. Patent No. 5,695,937).

SAGE provides the tool by which the expressed genes and the expression level of the genes of a cell at any one point in the cell cycle and under various environmental stimuli are isolated, sequenced and cataloged. SAGE provides quantitative gene expression data without the prerequisite of a hybridization probe for each transcript. SAGE is based on two principles. First, a short sequence tag (9-11 base pairs) contains sufficient information to uniquely identify a transcript, provided that it is derived from a defined location within that transcript. Second, many transcript tags can be concatenated into a single molecule and then sequenced, revealing the identity of multiple tags simultaneously. The expression pattern of any population of transcripts can be quantitatively evaluated by determining the abundance of individual tags and identifying the gene corresponding to each tag. Velculescu. et al. (1995) supra at 484.

Isolation and characterization of macromolecules of the invention

In one embodiment, the present invention provides isolation and characterization of costimulatory factors preferentially or differentially expressed in APCs such as monocyte-derived dendritic cells. SAGE analysis, as described above, can be used to identify a population of sequence tags corresponding to gene transcripts that are preferably or differentially expressed in dendritic cells but not in their monocyte precursor cells. In one aspect, the transcript or gene is previously identified but was heretofore unknown to be preferentially or

differentially expressed in monocyte-derived dendritic cells. In another embodiment, the transcript or gene disclosed herein is "novel", which means the tag or its respective complement does not comprise sequence of or correspond to a previously identified expressed sequence tag (EST) or characterized gene.

As one non-exclusive example, SAGE analysis has revealed that the chemokines PARC and TARC (Pulmonary and Activation-Regulated Chemokine, Hieshima, et al. (1997) J. Imm. 159(3):1140-1149 and Thymus and Activation-Regulated Chemokine, Imai, et al. (1996) J. Biol. Chem. 271(35):21514-21521) known for capability to recruit activated T cells, are differentially expressed by monocyte-derived immature dendritic cells, a fact that has not been appreciated prior to the present invention.

In a separate embodiment of the invention, the immunostimulatory factor as claimed can be a co-stimulatory factor that is differentially expressed in monocyte-derived DCs. The costimulatory factor used herein will include at least a portion of the protein sufficient to allow binding to its costimulatory ligand expressed on corresponding T cell surface.

According to an alternative embodiment of the invention, genes encoding transcription factors capable of upregulating the expression and activity of above-discussed costimulatory factors are used. The encoded transcription factors can be naturally occurring proteins involved in gene regulation pathways for the differentially expressed costimulatory factors in dendritic cells. Examples of transcription factors include: Nuclear Factor kappa B (NFκB) [Grohmann et al., (1998), Immunity 9(3) p. 315-323], X61498; the rel family of proteins notably relB [Wu et al., (1998) Immunity 9(6) p. 839-847]; CCAAT/enhancer binding protein [Yamanaka et al., (1998) Bioorganic and Medicinal Chemistry Letters 1(1) p. 213-221] YI 1525; inteferon-stimulated gene factor 3 (ISGF-3) [Schindler et al., 1992 P.N.A.S. USA 89(16) p. 7836-7839] M97935; STAT5 [Welte et al., (1997) European Journal of Immunology 27(10) p. 2737-2740], U43185; and NFAT-X [Masuda et al., 1995 Molecular and Cellular Biology 15(5) p. 2697-2706] U14510. Alternatively, the nucleotides encoding transcription factors can be

engineered via recombinant DNA technology. When included in a vaccine of the present invention, these nucleotides are capable of producing transcription factors that will transactivate the expression of the endogenous genes.

Thus, according to one embodiment of the invention, the immunostimulatory factor as claimed can be a transcription factor regulating the gene expression of a co-stimulatory factor differentially expressed in monocyte-derived DCs.

Differential gene expression analysis would also be expected to reveal genes encoding cell surface proteins that are preferentially expressed by either immature or mature dendritic cells as compared to monocyte precursors. Examples of such dendritic cell surface proteins that would be targets for activating ligands or engineered binding molecules (such as antibodies) include: IFN alpha/beta receptor X89814; IL-13 receptor Y09328; CD27 ligand L08096; CDlb M28826; CD151 D29963; CD53 M60871; LFA-1 M15395; and WSX1 cytokine receptor AF053004. These cell surface molecules may play a pivotal role in the function of dendritic cells by acting as co-stimulatory signals or modulators of DC function or migration. Naturally occurring ligands specific for these cell surface molecules or recombinant proteins (such as an antibody) generated to have specificity for these cell surface molecules might be expected to interact with the cell surface protein to stimulate the function of the dendritic cells or foster the maintenance of an activated state or stimulate the migration of dendritic cells to sites rich in T cells. Thus, the present invention relates to vaccines in which a gene or genes encoding tumor antigen or antigens is linked to a gene or genes encoding secreted proteins that have the capacity to bind to and modulate the activity of cell surface proteins identified as being differentially expressed in either mature or immature dendritic cells by comparative gene expression analysis (such as SAGE). In this manner, a novel autocrine loop is established whereby a genetically modified APC produces a ligand that is secreted from the APC where it can bind to cell surface receptors on that cell and stimulate the genetically modified dendritic cell.

In accordance with the present invention, the polynucleotide sequence encoding a tumor antigens and the polynucleotide sequence encoding an immunostimulatory factor can be constructed as separate molecules in the vaccine composition of the invention. Alternatively, the two nucleotide sequences can be covalently linked to form a single polynucleotide construct using standard recombinant DNA technology or chemical synthesis method. A recombinant DNA construct can be designed to have the linked sequences under the control of one transcriptional control region that can mediate the expression of both the tumor antigen and the immunostimulatory factor in a vaccine composition.

The invention also encompasses polynucleotides which differ from that of the polynucleotides described above, but encode substantially the same amino acid sequences. These altered, but phenotypically equivalent polynucleotides are referred to as "functionally equivalent nucleic acids." As used herein, "functionally equivalent nucleic acids" encompass nucleic acids characterized by slight and non-consequential sequence variations that will function in substantially the same manner to produce the same protein product(s) as the nucleic acids disclosed herein (e.g. by virtue of the degeneracy of the genetic codes), or that have conservative amino acid variations. For example, conservative variations include substitution of a non-polar residue with another non-polar residue, or substitution of a charged residue with a similarly charged residue. These sequence variations include those recognized by artisans in the art as those that do not substantially alter the tertiary structure of the encoded protein.

The polynucleotides of the invention can comprise additional sequences, such as additional coding sequences within the same transcription unit, controlling elements such as promoters, ribosome binding sites, and polyadenylation sites, additional transcription units under control of the same or a different promoter, sequences that permit cloning, expression, and transformation of a host cell, and any such construct as may be desirable to provide embodiments of this invention.

Indeed, this invention also provides a promoter sequence derived from cell's genome, wherein the promoter sequence corresponds to the regulatory region of a gene that is differentially transcribed in the cell as compared to a control cell. The promoters are identified and characterized by: l) probing a cDNA library with a probe corresponding to the SAGE tag sequence or generating a portion of the desired cDNA by conducting anchored PCR using primers based on the SAGE tag sequence. Examples of cell types wherein differential expression of a gene is related to promoter function include using the partial cDNA product obtained in step one above as a probe. cloning the extreme 5' end of the cDNA, and also by using the 5' end of the cDNA as a probe. cloning from a genomic library the promoter of the gene that encodes the cDNA. These promoters are identified using the methods described below in combination with standard molecular techniques. Functionally equivalent sequences, as defined above, are further provided by this invention.

In one aspect, the promoter is a sequence derived from an APC genome, wherein the promoter region corresponds to the regulatory region of a gene that is differentially transcribed in the APC. In a further aspect, the APC is a TNF-α treated dendritic cell. In a yet further aspect, the APC is an immature dendritic cell. In a still further aspect, the expression of genes from these two cell sources are compared to genes expressed in monocytes from which the dendritic cell populations were derived.

The promoters identified above can be operatively linked to a foreign polynucleotide to compel differential transcription of the foreign polynucleotide in the cell from which the promoter was derived. A foreign polynucleotide is intended to include any sequence which encodes in whole or in part a polypeptide or protein. It also includes sequences encoding ribozymes and antisense molecules.

Foreign polynucleotides also include therapeutic genes that encode dominant inhibitory oligonucleotides and peptides as well as genes that encode regulatory proteins and oligonucleotides. Generally, gene therapy will involve the

transfer of a single therapeutic gene although more than one gene may be necessary for the treatment of particular diseases. In one embodiment, the therapeutic gene is a dominant inhibiting mutant of the wild-type immunosuppressive agent. Alternatively, the therapeutic gene could be a wild-type copy of a defective gene or a functional homolog.

In one aspect, a tag identified in the Table corresponds to or comprises a polynucleotide that encodes a polypeptide or protein that is biologically active as an antigen, e.g., a native antigen, an altered antigen, a self-antigen or a tumor-associated antigen. Antigens are identified by noting the overexpression or cell-specific expression of a tag identified herein. Using the methods described below, the gene comprising or corresponding to the tag is identified. cloned and inserted into an APC. The tag corresponds to an antigen if a CTL response is raised under appropriate experimental conditions. The peptide is confirmed immunogeneic if an appropriate immune response is elecited.

The invention also encompasses co-administration of an immunostimulatory factor and a foreign polynucleotide, both under the control of promoters. In one embodiment, the promoter is an APC specific promoter. In alternative embodiment, the promoters are specific to tissue identified in the Table. The immunostimulatory factors of this invention include any polypeptide factors that modulate immune responses mediated by APC and corresponding T cells. For example, co-stimulatory factors that are differentially expressed in APCs can be used directly to boost the APC functions *in vivo*. Co-stimulatory factors have been described above.

The polynucleotides of the invention can be introduced and expressed in a suitable host cell for generating a cell-based vaccine. These methods are described in more detail below.

The polynucleotides and seqeunces identifed above can be conjugated to a detectable market, e.g., an enzymatic label or a radioisotope for detection of nucleic acid and/or expression of the gene in a cell. A wide variety of appropriate detectable markers are known in the art, including fluorescent. radioactive.

enzymatic or other ligands, such as avidin/biotin, which are capable of giving a detectable signal. In preferred embodiments, one will likely desire to employ a fluorescent label or an enzyme tag, such as urease, alkaline phosphatase or peroxidase, instead of radioactive or other environmental undesirable reagents. In the case of enzyme tags, colorimetric indicator substrates are known which can be employed to provide a means visible to the human eye or spectrophotometrically, to identify specific hybridization with complementary nucleic acid-containing samples.

The polynucleotides and sequences embodied in this invention can be obtained using chemical synthesis, recombinant cloning methods, PCR, or any combination thereof. Methods of chemical polynucleotide synthesis are well known in the art and need not be described in detail herein. One of skill in the art can use the sequence data provided herein to obtain a desired polynucleotide by employing a DNA synthesizer or ordering from a commercial service.

The polynucleotides and sequences of this invention can be inserted into a suitable vector, and the vector in turn can be introduced into a suitable host cell for replication and/or amplification. Polynucleotides can be introduced into host cells by any means known in the art. Cells are transformed by introducing an exogenous polynucleotide by direct uptake, endocytosis, transfection, f-mating or electroporation. Once introduced, the exogenous polynucleotide can be maintained within the cell as a non-integrated vector (such as a plasmid) or integrated into the host cell genome. Amplified DNA can be isolated from the host cell by standard methods. See, e.g., Sambrook et al. (1989) *supra*. RNA can also be obtained from transformed host cell, or it can be obtained directly from the DNA by using a DNA-dependent RNA polymerase.

The present invention further encompasses a variety of gene delivery vehicles comprising the polynucleotide of the present invention. Gene delivery vehicles include both viral and non-viral vectors such as naked plasmid DNA or DNA/liposome complexes. Vectors are generally categorized into cloning and expression vectors. Cloning vectors are useful for obtaining replicate copies of

the polynucleotides they contain, or as a means of storing the polynucleotides in a depository for future recovery. Expression vectors (and host cells containing these expression vectors) can be used to obtain polypeptides produced from the polynucleotides they contain. Suitable cloning and expression vectors include any known in the art, e.g., those for use in bacterial, mammalian. yeast and insect expression systems. The polypeptides produced in the various expression systems are also within the scope of the invention and are described above

When the vectors are used for gene therapy *in vivo* or ex *vivo*, a pharmaceutically acceptable vector is preferred, such as a replication-incompetent retroviral or adenoviral vector. Pharmaceutically acceptable vectors containing the nucleic acids of this invention can be further modified for transient or stable expression of the inserted polynucleotide. As used herein, the term "pharmaceutically acceptable vector" includes, but is not.limited to, a vector or delivery vehicle having the ability to selectively target and introduce the nucleic acid into dividing cells. An example of such a vector is a "replication-incompetent" vector defined by its inability to produce viral proteins, precluding spread of the vector in the infected host cell. An example of a replication-incompetent retroviral vector is LNL6 (Miller A.D. et al. (1989) BioTechniques 7:980-990). The methodology of using replication-incompetent retroviruses for retroviral-mediated gene transfer of gene markers is well established (Correll et al. (1989) Proc. Natl. Acad. Sci. USA 86:8912; Bordignon (1989) Proc. Natl. Acad. Sci. USA 86:8912-52; Culver K. (1991) Proc. Natl. Acad. Sci. USA **88**:3155; and Rill, D.R. (1991) Blood **79(10)**:2694. Clinical investigations have shown that there are few or no adverse effects associated with the viral vectors, see Anderson (1992) Science **256**:808-13.

Compositions containing the polynucleotides and sequences of this invention, in isolated form or contained within a vector or host cell are further provided herein. When these compositions are to be used pharmaceutically, they are combined with a pharmaceutically acceptable carrier.

A vector of this invention can contain one or more polynucleotides comprising a sequence shown in the Table or its complement. It can also contain polynucleotide sequences encoding other polypeptides that enhance, facilitate, or modulate the desired result, such as fusion components that facilitate protein purification, and sequences that increase immunogenicity of the resultant protein or polypeptide.

Also embodied in the present invention are host cells transformed with the vectors as described above. Both prokaryotic and eukaryotic host cells may be used. Prokaryotic hosts include bacterial cells, for example *E. coli* and *Mycobacteria*. Among eukaryotic hosts are yeast, insect, avian. plant and mammalian cells. Host systems are known in the art and need not be described in detail herein. Examples of mammalian host cells include but not limited to COS, HeLa, and CHO cells, and APCs, e.g., dendritic cells.

The host cells of this invention can be used, inter alia. as repositories of polynucleotides differentially expressed in a cell or as vehicles for production of the polynucleotides and the encoded polypeptides.

Polypeptides of the Invention

This invention provides a population of proteins or polypeptides expressed from the population of polynucleotides of this invention, which is intended to include wild-type and recombinantly produced polypeptides and proteins from prokaryotic and eukaryotic host cells, as well as muteins, analogs, fusions and fragments thereof. In some embodiments, the term also includes antibodies and anti-idiotypic antibodies.

It is understood that equivalents or variants of the wild-type polypeptide or protein also are within the scope of this invention. An "equivalent" varies from the wild-type sequence encoded by the polynucleotides of the invention by any combination of additions, deletions, or substitutions while preserving at least one functional property of the fragment relevant to the context in which it is being used. For instance, an equivalent of a polypeptide of the invention may have the

ability to elicit an immune response with a similar antigen specificity as that elicited by the wild-type polypeptide. As is apparent to one skilled in the art, the equivalent may also be associated with, or conjugated with, other substances or agents to facilitate, enhance, or modulate its function.

The invention includes modified polypeptides containing conservative or non-conservative substitutions that do not significantly affect their properties, such as the immunogenicity of the peptides or their tertiary structures. Modification of polypeptides is routine practice in the art. Amino acid residues which can be conservatively substituted for one another include but are not limited to: glycine/alanine; valine/isoleucine/leucine; asparagine/glutamine; aspartic acid/glutamic acid; serine/threonine; lysine/arginine: and phenylalanine/tyrosine. These polypeptides also include glycosylated and nonglycosylated polypeptides, as well as polypeptides with other post-translational modifications, such as, for example, glycosylation with different sugars, acetylation, and phosphorylation.

The polypeptides of the invention can also be conjugated to a chemically functional moiety. Typically, the moiety is a label capable of producing a detectable signal. These conjugated polypeptides are useful, for example, in detection systems such as imaging of breast tumor. Such labels are known in the art and include, but are not limited to, radioisotopes, enzymes, fluorescent compounds, chemiluminescent compounds, bioluminescent compounds substrate cofactors and inhibitors. See, for examples of patents teaching the use of such labels, U.S. Patent Nos. 3,817,837; 3,850,752; 3,939,350; 3,996,345; 4,277,437: 4,275,149; and 4,366,241. The moieties can be covalently linked to the polypeptides, recombinantly linked, or conjugated to the polypeptides through a secondary reagent, such as a second antibody, protein A, or a biotin-avidin complex.

Other functional moieties include agents that enhance immunological reactivity, agents that facilitate coupling to a solid support, vaccine carriers, bioresponse modifiers, paramagnetic labels and drugs. Agents that enhance

immunological reactivity include, but are not limited to, bacterial superantigens. Agents that facilitate coupling to a solid support include, but are not limited to, biotin or avidin. Immunogen carriers include, but are not limited to, any physiologically acceptable buffers.

The invention also encompasses fusion proteins comprising polypeptides encoded by the polynucleotides disclosed herein and fragments thereof. Such fusion may be between two or more polypeptides of the invention and a related or unrelated polypeptide. Useful fusion partners include sequences that facilitate the intracellular localization of the polypeptide, or enhance immunological reactivity or the coupling of the polypeptide to an immunoassay support or a vaccine carrier. For instance, the polypeptides can be fused with a bioresponse modifier. Examples of bioresponse modifiers include, but are not limited to, fluorescent proteins such as green fluorescent protein (GFP), cytokines or lymphokines such as interleukin-2 (IL-2), interleukin 4 (IL-4), GM-CSF, and α-interferon. Another useful fusion sequence is one that facilitates purification. Examples of such sequences are known in the art and include those encoding epitopes such as Myc, HA (derived from influenza virus hemagglutinin), His-6, or FLAG. Other fusion sequences that facilitate purification are derived from proteins such as glutathione S-transferase (GST), maltose-binding protein (MBP), or the Fc portion of immunoglobulin. For immunological purposes, tandemly repeated polypeptide segments may be used as antigens, thereby producing highly immunogenic proteins.

The proteins of this invention also can be combined with various liquid phase carriers, such as sterile or aqueous solutions, pharmaceutically acceptable carriers, suspensions and emulsions. Examples of non-aqueous solvents include propyl ethylene glycol, polyethylene glycol and vegetable oils. When used to prepare antibodies, the carriers also can include an adjuvant that is useful to non-specifically augment a specific immune response. A skilled artisan can easily determine whether an adjuvant is required and select one. However, for the

purpose of illustration only, suitable adjuvants include, but are not limited to Freund's Complete and Incomplete, mineral salts and polynucleotides.

The proteins and polypeptides of this invention are obtainable by a number of processes well known to those of skill in the art. which include purification, chemical synthesis and recombinant methods. Full-length proteins can be purified from a cell derived from non-metastatic or metastatic breast tumor tissue or tissue lysate by methods such as immunoprecipitation with antibody, and standard techniques such as gel filtration, ion-exchange. reversed-phase, and affinity chromatography using a fusion protein as shown herein. For such methodology, see for example Deutscher et al. (1999) GUIDE TO PROTEIN PURIFICATION: METHODS IN ENZYMOLOGY (Vol . 182, Academic Press). Accordingly, this invention also provides the processes for obtaining these proteins and polypeptides as well as the products obtainable and obtained by these processes.

The proteins and polypeptides also can be obtained by chemical synthesis using a commercially available automated peptide synthesizer such as those manufactured by Perkin Elmer/Applied Biosystems, Inc., Model 430A or 431A, Foster City, CA, USA. The synthesized protein or polypeptide can be precipitated and further purified, for example by high performance liquid chromatography (HPLC). Accordingly, this invention also provides a process for chemically synthesizing the proteins of this invention by providing the sequence of the protein and reagents, such as amino acids and enzymes and linking together the amino acids in the proper orientation and linear sequence.

Alternatively, the proteins and polypeptides can be obtained by well-known recombinant methods as described, for example, in Sambrook et al. (1989), *supra,* using the host cell and vector systems described above.

Antibodies

Also provided by this invention is a population of antibodies capable of specifically binding to the proteins or polypeptides as described above. The

antibodies of the present invention encompass polyclonal antibodies and monoclonal antibodies. They include but are not limited to mouse, rat, and rabbit or human antibodies. This invention also encompasses functionally equivalent antibodies and fragments thereof. As used herein with respect to the exemplified antibodies, the phrase "functional equivalent" means an antibody or fragment thereof, or any molecule having the antigen binding site (or epitope) of the antibody that cross-blocks an exemplified antibody when used in an immunoassay such as immunoblotting or immunoprecipitation.

Antibody fragments include the Fab, Fab', $F(ab')_2$, and Fv regions, or derivatives or combinations thereof. Fab, Fab', and $F(ab')_2$ regions of an immunoglobulin may be generated by enzymatic digestion of the monoclonal antibodies using techniques well known to those skilled in the art. Fab fragments may be generated by digesting the monoclor al antibody with papain and contacting the digest with a reducing agent to reductively cleave disulfide bonds. Fab' fragments may be obtained by digesting the antibody with pepsin and reductive cleavage of the fragment so produce with a reducing agent. In the absence of reductive cleavage, enzymatic digestion of the monoclonal with pepsin produces $F(ab')_2$ fragments.

It will further be appreciated that encompassed within the definition of antibody fragment is single chain antibody that can be generated as described in U.S. 4,704,692, as well as chimeric antibodies and humanized antibodies (Oi et al. (1986) BioTechniques **4(3)**:214). Chimeric antibodies are those in which the various domains of the antibodies' heavy and light chains are coded for by DNA from more than one species.

As used herein with regard to the monoclonal antibody, the "hybridoma cell line" is intended to include all derivatives, progeny cells of the parent hybridoma that produce the monoclonal antibodies specific for the polypeptides of the present invention, regardless of generation of karyotypic identity.

Laboratory methods for producing polyclonal antibodies and monoclonal antibodies, as well as deducing their corresponding nucleic acid sequences, are

known in the art, see Harlow and Lane (1988) *supra* and Sambrook et al. (1989) *supra*. For production of polyclonal antibodies, an appropriate host animal is selected, typically a mouse or rabbit. The substantially purified antigen, whether the whole transmembrane domain, a fragment thereof, or a polypeptide corresponding to a segment of or the entire specific loop region within the transmembrane domain, coupled or fused to another polypeptide, is presented to the immune system of the host by methods appropriate for the host. The antigen is introduced commonly by injection into the host footpads, via intramuscular, intraperitoneal, or intradermal routes. Peptide fragments suitable for raising antibodies may be prepared by chemical synthesis, and are commonly coupled to a carrier molecule (e.g., keyhole limpet hemocyanin) and injected into a host over a period of time suitable for the production of antibodies. Alternatively, the antigen can be generated recombinantly as a fusion protein. Examples of components for these fusion proteins include, but are not limited to myc, HA, FLAG, His-6, glutathione S-transferease, maltose binding protein or the Fc portion of immunoglobulin.

The monoclonal antibodies of this invention refer to antibody compositions having a homogeneous antibody population. It is not intended to be limited as regards to the source of the antibody or the manner in which it is made. Generally, monoclonal antibodies are biologically produced by introducing protein or a fragment thereof into a suitable host, e.g., a mouse. After the appropriate period of time, the spleens of such animal is excised and individual spleen cells fused, typically, to immortalized myeloma cells under appropriate selection conditions. Thereafter the cells are clonally separated and the supernatants of each clone are tested for their production of an appropriate antibody specific for the desired region of the antigen using methods well known in the art.

The isolation of other hybridomas secreting monoclonal antibodies with the specificity of the monoclonal antibodies of the invention can also be accomplished by one of ordinary skill in the art by producing anti-idiotypic

antibodies (Herlyn et al. (1986) Science **232**:100). An anti-idiotypic antibody is an antibody which recognizes unique determinants present on the monoclonal antibody produced by the hybridoma of interest.

Idiotypic identity between monoclonal antibodies of two hybridomas demonstrates that the two monoclonal antibodies are the same with respect to their recognition of the same epitopic determinant. Thus, by using antibodies to the epitopic determinants on a monoclonal antibody it is possible to identify other hybridomas expressing monoclonal antibodies of the same epitopic specificity.

It is also possible to use the anti idiotype technology to produce monoclonal antibodies which mimic an epitope. For example, an anti-idiotypic monoclonal antibody made to a first monoclonal antibody will have a binding domain in the hypervariable region which is the mirror image of the epitope bound by the first monoclonal antibody. Thus, in this instance, the anti-idiotypic monoclonal antibody could be used for immunization for production of these antibodies.

Other suitable techniques of antibody production include, but are not limited to, *in vitro* exposure of lymphocytes to the antigenic polypeptides or selection of libraries of antibodies in phage or similar vectors. See Huse et al. (1989) Science **246**:1275-1281. Genetically engineered variants of the antibody can be produced by obtaining a polynucleotide encoding the antibody, and applying the general methods of molecular biology to introduce mutations and translate the variant. The above described antibody "derivatives" are further provided herein.

Sera harvested from the immunized animals provide a source of polyclonal antibodies. Detailed procedures for purifying specific antibody activity from a source material are known within the art. Undesired activity cross-reacting with other antigens, if present, can be removed, for example, by running the preparation over adsorbants made of those antigens attached to a solid phase and eluting or releasing the desired antibodies off the antigens. If desired, the specific antibody activity can be further purified by such techniques as protein A

chromatography, ammonium sulfate precipitation, ion exchange chromatography, high-performance liquid chromatography and immunoaffinity chromatography on a column of the immunizing polypeptide coupled to a solid support.

The specificity of an antibody refers to the ability of the antibody to distinguish polypeptides comprising the immunizing epitope from other polypeptides. An ordinary skill in the art can readily determine without undue experimentation whether an antibody shares the same specificity as a antibody of this invention by determining whether the antibody being tested prevents an antibody of this invention from binding the polypeptide(s) with which the antibody is normally reactive. If the antibody being tested competes with the antibody of the invention as shown by a decrease in binding by the antibody of this invention, then it is likely that the two antibodies bind to the same or a closely related epitope. Alternatively, one can pre-incubate the antibody of this invention with the polypeptide(s) with which it is normally reactive, and determine if the antibody being tested is inhibited in its ability to bind the antigen. If the antibody being tested is inhibited, then, in all likelihood, it has the same, or a closely related, epitopic specificity as the antibody of this invention.

The antibodies of the invention can be bound to many different carriers. Thus, this invention also provides compositions containing antibodies and a carrier. Carriers can be active and/or inert. Examples of well-known carriers include polypropylene, polystyrene, polyethylene, dextran, nylon, amylases, glass, natural and modified celluloses, polyacrylamides, agaroses and magnetite. The nature of the carrier can be either soluble or insoluble for purposes of the invention. Those skilled in the art will know of other suitable carriers for binding antibodies, or will be able to ascertain such, using routine experimentation.

The antibodies of this invention can also be conjugated to a detectable agent or a hapten. The complex is useful to detect the polypeptide(s) (or polypeptide fragments) to which the antibody specifically binds in a sample, using standard immunochemical techniques such as immunohistochemistry as described by Harlow and Lane (1988) *supra*. There are many different labels and

methods of labeling known to those of ordinary skill in the art. Examples of the types of labels which can be used in the present invention include radioisotopes, enzymes, colloidal metals, fluorescent compounds, bioluminescent compounds, and chemiluminescent compounds. Those of ordinary skill in the art will know of other suitable labels for binding to the antibody, or will be able to ascertain such, using routine experimentation. Furthermore, the binding of these labels to the antibody of the invention can be done using standard techniques common to those of ordinary skill in the art.

Another technique which may also result in greater sensitivity consists of coupling the antibodies to low molecular weight haptens. These haptens can then be specifically detected by means of a second reaction. For example, it is common to use such haptens as biotin, which reacts avidin, or dinitropherryl, pyridoxal, and fluorescein, which can react with specific anti-hapten antibodies. See Harlow and Lane (1988) *supra.*

Compositions containing the antibodies, fragments thereof or cell lines which produce the antibodies, are encompassed by this invention. When these compositions are to be used pharmaceutically, they are combined with a pharmaceutically acceptable carrier.

Uses of Polynucleotides, Polypeptides and Antibodies of the Invention

The polynucleotides, polypeptides and antibodies embodied in this invention provide specific reagents that can be used in standard diagnostic procedures. Accordingly, one embodiment of the present invention is a method of characterizing a cell of monocyte lineage by detecting differential expression of a polynucleotide comprising any one of the sequences shown in the Table or any one of the disclosed populations, or the encoded polypeptides.

In assaying for an alteration in mRNA level, nucleic acid contained in the aforementioned a sample suspected of containing a dendritic cell is first extracted according to standard methods in the art. For instance, mRNA can be isolated using various lytic enzymes or chemical solutions according to the procedures set

forth in Sambrook et al. (1989), *supra* or extracted by nucleic-acid-binding resins following the accompanying instructions provided by manufactures. The mRNA contained in the extracted nucleic acid sample is then detected by hybridization (e.g. Northern blot analysis) and/or amplification procedures according to methods widely known in the art or based on the methods exemplified herein.

Nucleic acid molecules having at least 10 nucleotides and exhibiting sequence complementarity or homology to the polynucleotides described herein find utility as hybridization probes. It is known in the art that a "perfectly matched" probe is not needed for a specific hybridization. Minor changes in probe sequence achieved by substitution, deletion or insertion of a small number of bases do not affect the hybridization specificity. In general, as much as 20% base-pair mismatch (when optimally aligned) can be tolerated. Preferably, a probe useful for detecting the aforementioned mRNA that is differentially expressed in the cell type for which one is probing. These tags are identified in Table 1, below. More preferably, the probe is at least 80%, or 85% identical to the corresponding gene sequence after alignment of the homologous region; even more preferably, it exhibits 90% identity.

These probes can be used in hybridization reaction (*e.g.* Southern and Northern blot analysis) to detect, prognose, diagnose or monitor the physiological states associated with the differential expression of these genes. The total size of fragment, as well as the size of the complementary stretches, will depend on the intended use or application of the particular nucleic acid segment. Smaller fragments derived from the known sequences will generally find use in hybridization embodiments, wherein the length of the complementary region may be varied, such as between about 10 and about 100 nucleotides, or even full length according to the complementary sequences one wishes to detect.

Nucleotide probes having complementary sequences over stretches greater than 10 nucleotides in length are generally preferred, so as to increase stability and selectivity of the hybrid, and thereby improving the specificity of particular hybrid molecules obtained. More preferably, one can design nucleic acid

molecules having gene-complementary stretches of more than 50 nucleotides in length, or even longer where desired. Such fragments may be readily prepared by, for example, directly synthesizing the fragment by chemical means, by application of nucleic acidreproduction technology, such as the PCR™ technology with two priming oligonucleotides as described in U.S. Pat. No. 4,603,102 or by introducing selected sequences into recombinant vectors for recombinant production. A preferred probe is about 50-75 or more preferably, 50-100, nucleotides in length.

In certain embodiments, it will be advantageous to employ nucleic acid sequences of the present invention in combination with an appropriate means, such as a label, for detecting hybridization and therefore complementary sequences. A wide variety of appropriate indicator means are known in the art, including fluorescent, radioactive, enzymatic or other ligands, such as avidin/biotin, which are capable of giving a detectable signal. In preferred embodiments, one will likely desire to employ a fluorescent label or an enzyme tag, such as urease, alkaline phosphatase or peroxidase, instead of radioactive or other environmental undesirable reagents. In the case of enzyme tags, colorimetric indicator substrates are known which can be employed to provide a means visible to the human eye or spectrophotometrically, to identify specific hybridization with complementary nucleic acid-containing samples.

The nucleotide probes of the present invention can also be used as primers and detection of genes or gene transcripts that are differentially expressed in certain body tissues. A preferred primer is one comprising a sequence of shown in the Table or their respective complements. Additionally, a primer useful for detecting the aforementioned gene or transcript is at least about 80% identical to the homologous region of comparable size of the gene or transcript to be detected contained in the previously identified sequences. For the purpose of this invention, amplification means any method employing a primer-dependent polymerase capable of replicating a target sequence with reasonable fidelity. Amplification may be carried out by natural or recombinant DNA-polymerases

such as T7 DNA polymerase, Klenow fragment of *E.coli* DNA polymerase, and reverse transcriptase.

A preferred amplification method is PCR. General procedures for PCR are taught in MacPherson et al., PCR: A PRACTICAL APPROACH, (IRL Press at Oxford University Press (1991)). However, PCR conditions used for each application reaction are empirically determined. A number of parameters influence the success of a reaction. Among them are annealing temperature and time, extension time, Mg^{2+} ATP concentration, pH, and the relative concentration of primers, templates, and deoxyribonucleotides.

After amplification, the resulting DNA fragments can be detected by agarose gel electrophoresis followed by visualization with ethidium bromide staining and ultraviolet illumination. A specific amplification of the gene or transcript of interest can be verified by demonstrating that the amplified DNA fragment has the predicted size, exhibits the predicated restriction digestion pattern, and/or hybridizes to the correct cloned DNA sequence.

The probes and tags of this invention also can be attached to a solid support for use in high throughput screening assays using methods known in the art. PCT WO 97/10365 and U.S. Patent numbers 5,405,783, 5,412,087 and 5,445,934, for example, disclose the construction of high density oligonucleotide chips which can contain one or more of the sequences disclosed herein. Based in the methods disclosed in U.S. Patent numbers 5,405,783, 5,412,087 and 5,445,934, the probes of this invention are synthesized on a derivatized glass surface. Photoprotected nucleoside phosphoramidites are coupled to the glass surface, selectively deprotected by photolysis through a photolithographic mask, and reacted with a second protected nucleoside phosphoramidite. The coupling/deprotection process is repeated until the desired probe is complete.

The expression level of a gene of interest is determined through exposure of a nucleic acid sample to the probe-modified chip. Extracted nucleic acid is labeled, for example, with a fluorescent tag, preferably during an amplification step. Hybridization of the labeled sample is performed at an appropriate

stringency level. The degree of probe-nucleic acid hybridization is quantitatively measured using a detection device, such as a confocal microscope. See U.S. Pat Nos. 5,578,832 and 5,631,734. The obtained measurement is directly correlated with gene expression level.

More specifically, the probes and high density oligonucleotide probe arrays provide an effective means of monitoring expression of a multiplicity of genes. The expression monitoring methods of this invention may be used in a wide variety of circumstances including detection of disease, identification of differential gene expression between two samples, or screening for compositions that upregulate or downregulate the expression of particular genes.

In another preferred embodiment, the methods of this invention are used to monitor expression of the genes which specifically hybridize to the probes of this invention in response to defined stimuli, such as a drug.

In one embodiment, the hybridized nucleic acids are detected by detecting one or more labels attached to the sample nucleic acids. The labels may be incorporated by any of a number of means well known to those of skill in the art. However, in one aspect, the label is simultaneously incorporated during the amplification step in the preparation of the sample nucleic acid. Thus, for example, polymerase chain reaction (PCR) with labeled primers or labeled nucleotides will provide a labeled amplification product. In a separate embodiment, transcription amplification, as described above, using a labeled nucleotide (e.g. fluorescein-labeled UTP and/or CTP) incorporates a label in to the transcribed nucleic acids.

Alternatively, a label may be added directly to the original nucleic acid sample (e.g., mRNA, polyA, mRNA, cDNA, etc.) or to the amplification product after the amplification is completed. Means of attaching labels to nucleic acids are well known to those of skill in the art and include, for example nick translation or end-labeling (e.g. with a labeled RNA) by kinasing of the nucleic acid and subsequent attachment (ligation) of a nucleic acid linker joining the sample nucleic acid to a label (e.g., a fluorophore).

The nucleic acid sample also may be modified prior to hybridization to the high density probe array in order to reduce sample complexity thereby decreasing background signal and improving sensitivity of the measurement using the methods disclosed in WO 97/10365.

Results from the chip assay are typically analyzed using a computer software program. See, for example, EP 0717 113 A2 and WO 95/20681. The hybridization data are read into the program, which calculates the expression level of the targeted gene(s). This figure is compared against existing data sets of gene expression levels for various cell types.

Expression of the genes associated characteristic of dendritic cells as compared to monocytes can also be determined by examining the protein product of the polynucleotides of the present invention. Determining the protein level involves a) providing a biological sample containing polypeptides; and (b) measuring the amount of any immunospecific binding that occurs between an antibody reactive to the protein products of interest and a component in the sample, in which the amount of immunospecific binding indicates the level of the protein products.

A variety of techniques are available in the art for protein analysis. They include but are not limited to radioimmunoassays, ELISA (enzyme linked immunoradiometric assays), "sandwich" immunoassays, immunoradiometric assays, in situ immunoassays (using *e.g.*, colloidal gold, enzyme or radioisotope labels), western blot analysis, immunoprecipitation assays, immunofluorescent assays, and SDS-PAGE. In addition, cell sorting analysis can be employed to detect cell surface antigens. Such analysis involves labeling target cells with antibodies coupled to a detectable agent, and then separating the labeled cells from the unlabeled ones in a cell sorter. A sophisticated cell separation method is fluorescence-activated cell sorting (FACS). Cells traveling in single file in a fine stream are passed through a laser beam, and the fluorescence of each cell bound by the fluorescently labeled antibodies is then measured.

Antibodies that specifically recognize and bind to the protein products of interest are required for conducting the aforementioned protein analyses. These antibodies may be purchased from commercial vendors or generated and screened using methods well known in the art. See Harlow and Lane (1988) *supra.* and Sambrook et al. (1989) *supra.*

There are various methods available in the art for quantifying mRNA or protein level from a cell sample and indeed, any method that can quantify these levels is encompassed by this invention. For example, determination of the mRNA level of the gene may involve, in one aspect, measuring the amount of mRNA in a mRNA sample isolated from the cell by hybridization or quantitative amplification using at least one oligonucleotide probe that is complementary to the mRNA. Determination of the aforementioned protein products requires measuring the amount of immunospecific binding that occurs between an antibody reactive to the product of interest. To detect and quantify the immunospecific binding, or signals generated during hybridization or amplification procedures, digital image analysis systems including but not limited to those that detect radioactivity of the probes or chemiluminescence can be employed.

The promoter sequences of this invention are useful for targeted expression of foreign polynucleotides. The promoters can be operatively linked to foreign polynucleotides and administered to patients alone or after transduction into host cells. Because the promoters have been selected for cell-specific expression, after incorporation into host cells, either *in* vivo or *ex vivo,* targeted expression of the inserted polynucleotide can be obtained.

In one embodiment, the promoters preferentially express operatively linked polynucleotides in APCs, e.g., tumor associated antigens. Genes coding for immunostimulatory molecules such as cytokines or co-stimulatory molecules can be linked to the promoter sequence and gene coding for the antigen. Administration of these polynucleotides to a subject, alone or transduced into host

APCs, are useful to induce an immune response by educating immune effector cells *in vivo*.

Screening Assays

The present invention also provides a screen for various agents which modulate the expression of a polynucleotide associated the phenotype of a normal or pathological cell by first contacting a suitable cell with an effective amount of a potential agent, and then assaying for a change in the expression level of a polynucleotide selected from the group consisting of SEQ ID NOS: 1-207 or any one of the populations from which the population was derived. For example, one would assay for a change in the expression level of any one of the polynucleotides comprising or corresponding to the sequence shown in the table in a monocyte or dendritic cell. A change in the expression level is indicative of a candidate modulating agent. In certain aspects of the invention, an agent may result in phenotypic changes of the recipient cell as evidenced by an agent-induced cell apoptosis, a reduced rate of cell growth or cell motility. Altered gene expression can be detected by assaying for altered mRNA expression or protein expression using the probes, primers and antibodies as described herein.

To practice the method *in vitro*, cell cultures or tissue cultures previously identified as expressing one or more of the tags or polypeptides corresponding to the tags are first provided. The cell can be a cultured cell or a genetically modified cell in which a transcript from the Table, or their complements, or alternatively, transcripts which contain or correspond to a tag or its respective complement is expressed. The cells are cultured under conditions (temperature, growth or culture medium and gas (CO_2)) and for an appropriate amount of time to attain exponential proliferation without density dependent constraints. It also is desirable to maintain an additionalseparate cell culture; one which does not receive the agent being tested as a control.

As is apparent to one of skill in the art, suitable cells may be cultured in microtiter plates and several agents may be assayed at the same time by noting genotypic changes and/or phenotypic changes.

When the agent is a composition other than naked DNA or RNA, the agent may be directly added to the cell culture or added to culture medium for addition. As is apparent to those skilled in the art, an "effective" amount must be added which can be empirically determined. When the agent is a polynucleotide, it may be introduced directly into a cell by transfection or electroporation. Alternatively, it may be inserted into the cell using a gene delivery vehicle or other methods as described above.

For the purposes of this invention, an "agent" is intended to include, but not be limited to a biological or chemical compound such as a simple or complex organic or inorganic molecule, a peptide, a protein (e.g. antibody) or a polynucleotide (e.g. anti-sense). A vast array of compounds can be synthesized, for example polymers, such as polypeptides and polynucleotides, and synthetic organic compounds based on various core structures, and these are also included in the term "agent." In addition, various natural sources can provide compounds for screening, such as plant or animal extracts, and the like. It should be understood, although not always explicitly stated that the agent is used alone or in combination with another agent, having the same or different biological activity as the agents identified by the inventive screen. The agents and methods also are intended to be combined with other therapies.

The assays also can be performed in a subject. When the subject is an animal such as a rat, mouse or simian, the method provides a convenient animal model system which can be used prior to clinical testing of an agent. In this system, a candidate agent is a potential drug if transcript expression is altered, i.e., upregulated (such as restoring tumor suppressor function), downregulated or eliminated as with drug resistant genes or oncogenes, or if symptoms associated or correlated to the presence of cells containing transcript expression are ameliorated, each as compared to untreated, animal having the pathological cells.

It also can be useful to have a separate negative control group of cells or animals which are healthy and not treated, which provides a basis for comparison. After administration of the agent to subject, suitable cells or tissue samples are collected and assayed for altered gene expression.

These agents of this invention and the above noted compounds and their derivatives can be combined with a pharmaceutically acceptable carrier for the preparation of medicaments for use in the methods described herein.

The agents of the present invention can be administered to a cell or a subject by various delivery systems known in the art. Non-limiting examples include encapsulation in liposomes, microparticles, microcapsules, expression by recombinant cells, receptor-mediated endocytosis (see, *e.g.*, Wu and Wu (1987) J. Biol. Chem. 262:4429-4432), and construction of a therapeutic nucleic acid as part of a retroviral or other vector. Methods of delivery include but are not limited to transdermally, gene therapy, intra-arterial, intra-muscular, intravenous, intranasal, and oral routes, and include sustained delivery systems. In a specific embodiment, it may be desirable to administer the pharmaceutical compositions of the invention locally to the area in need of treatment; this may be achieved by, for example, and not by way of limitation, local infusion during surgery, by injection, or by means of a catheter or targeted gene delivery of the sequence coding for the therapeutic.

Administration *in vivo* can be effected in one dose, continuously or intermittently throughout the course of treatment. Methods of determining the most effective means and dosage of administration are well known to those of skill in the art and will vary with the composition used for therapy, the purpose of the therapy, the target cell being treated, and the subject being treated. Single or multiple administrations can be carried out with the dose level and pattern being selected by the treating physician. Suitable dosage formulations and methods of administering the agents can be found below.

The agents and compositions of the present invention can be used in the manufacture of medicaments and for the treatment of humans and other animals

by administration in accordance with conventional procedures, such as an active ingredient in pharmaceutical compositions.

The pharmaceutical compositions can be administered orally, intranasally, parenterally, transdermally or by inhalation therapy, and may take the form of tablets, lozenges, granules, capsules, pills, ampoules, suppositories or aerosol form. They may also take the form of gene therapy, suspensions, solutions and emulsions of the active ingredient in aqueous or nonaqueous diluents, syrups, granulates or powders. In addition to an agent of the present invention, the pharmaceutical compositions can also contain other pharmaceutically active compounds or a plurality of compounds of the invention.

It should be understood that in addition to the ingredients particularly mentioned above, the formulations of this invention may include other agents conventional in the art having regard to the type of formulation in question, for example, those suitable for oral administration may include such further agents as sweeteners, thickeners and flavoring agents. It also is intended that the agents, compositions and methods of this invention be combined with other suitable compositions and therapies.

Genomics Applications

This invention also provides a process for preparing a database for the analysis of a cell's expressed genes by storing in a digital storage medium information related to the sequences of the transcriptome. Using this method, a data processing system for standardized representation of the expressed genes of a cell is compiled. The data processing system is useful to analyze gene expression between two cells by first selecting a cell and then identifying and sequencing the transcriptome of the cell. This information is stored in a computer-readable storage medium as the transcriptome. The transcriptome is then compared with at least one sequence(s) of transcription fragments from a reference cell. The compared sequences are then analyzed. Uniquely expressed sequences and

sequences differentially expressed between the reference cell and the selected cell can be identified by this method.

In other words, this invention provides a computer based method for screening the homology of an unknown DNA or mRNA sequence against one or more of transcribed or expressed genes of a preselected cell by first providing the complete set of expressed genes, i.e., the transcriptome, in computer readable form and homology screening the DNA or mRNA of the unknown sequence against transcriptome and determining whether the DNA sequence of the unknown contains similarities to any portion of the transcriptome listed in the computer readable form. In one embodiment, SEQ ID Nos. or polynucleotides corresponding to these sequences are the transcriptome against which test cells are compared.

Thus, the information provided herein also provides a means to compare the relative abundance of gene transcripts in different biological specimens by use of high-throughput sequence-specific analysis of individual RNAs or their corresponding cDNAs using a modification of the systems described in WO 95/2068, 96/23078 and 5,618,672.

The tags or transcripts also can be attached to a solid support for use in high throughput screening assays. PCT WO 97/10365, for example, discloses the construction of high density oligonucleotide chips. See also, U.S. Patent Nos. 5,405,783, 5,412,087 and 5,445,934. Using this method, the probes are synthesized on a derivatized glass surface. Photoprotected nucleoside phosphoramidites are coupled to the glass surface, selectively deprotected by photolysis through a photolithographic mask, and reacted with a second protected nucleoside phosphoramidite. The coupling/deprotection process is repeated until the desired probe is complete.

The expression level of a gene is determined through exposure of a nucleic acid sample to the probe-modified chip. Extracted nucleic acid is labeled, for example, with a fluorescent tag, preferably during an amplification step. Hybridization of the labeled sample is performed at an appropriate stringency

level. The degree of probe-nucleic acid hybridization is quantitatively measured using a detection device, such as a confocal microscope. See U.S. Patent Nos. 5,578,832 and 5,631,734. The obtained measurement is directly correlated with gene expression level.

Results from the chip assay are typically analyzed using a computer software program. See, for example, EP 0717 113 A2 and WO 95/20681. The hybridization data is read into the program, which calculates the expression level of the targeted gene(s). This figure is compared against existing data sets of gene expression levels for that cell type.

Additional utilities of the database include, but are not limited to analysis of the developmental state of a test cell, the influence of viral or bacterial infection, control of cell cycle, effect of a tumor suppressor gene or lack thereof, polymorphism within the cell type, apoptosis, and the effect of regulatory genes.

Non-Human Transgenic Animals

In another aspect, the novel polynucleotide sequences associated with a pathological state of a cell can be used to generate transgenic animal models. In recent years, geneticists have succeeded in creating transgenic animals, for example mice, by manipulating the genes of developing embryos and introducing foreign genes into these embryos. Once these genes have integrated into the genome of the recipient embryo, the resulting embryos or adult animals can be analyzed to determine the function of the gene. The mutant animals are produced to understand the function of known genes *in vivo* and to create animal models of human diseases. *(see, e.g.,* Chisaka *et al.* (1992) 355:5 1 6-520; Joyner et al. (1 992) in POSTIMPLANTATION DEVELOPMENT IN THE MOUSE (Chadwick and Marsh, eds., John Wiley & Sons, United Kingdom) pp:277-297; Dorin et al. (1992) Nature 359:211-215).

The following examples are intended to illustrate, but not limit, the invention.

Cloning Techniques

The following are several techniques available to the skilled artisan for identification and cloning of the polynucleotides corresponding to the tags having the sequences set forth in the Table.

5

I) *RACE-PCR Technique*

One method to isolate the gene or cDNA which codes for a polypeptide or protein involves the 5'-RACE-PCR technique. In this technique, the poly-A mRNA that contains the coding sequence of particular interest is first identified 10 by hybridization to a sequence disclosed herein and then reverse transcribed with a 3'-primer comprising the sequence disclosed herein. The newly synthesized cDNA strand is then tagged with an anchor primer of a known sequence, which preferably contains a convenient cloning restriction site attached at the 5' end. The tagged cDNA is then amplified with the 3'-primer (or a nested primer sharing 15 sequence homology to the internal sequences of the coding region) and the 5'-anchor primer. The amplification may be conducted under conditions of various levels of stringency to optimize the amplification specificity. 5'RACE-PCR can be readily performed using commercial kits (available from, e.g., BRL 5 Life Technologies Inc., Clontech) according to the manufacturer's instructions.

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2) *Isolation of partial cDNA (3 'fragment) by 3 'directed PCR reaction*

This procedure is a modification of the protocol described in Polyak et al. (1997) Nature 389:300. Briefly, the procedure uses SAGE tags in PCR reaction such that the resultant PCR product contains the SAGE tag of interest as well as 25 additional cDNA, the length of which is defined by the position of the tag with respect to the 3' end of the cDNA. The cDNA product derived from such a transcript driven PCR reaction can be used for many applications.

RNA from a source believed to express the cDNA corresponding to a given tag is first converted to double-stranded cDNA using any standard cDNA 30 protocol. Similar conditions used to generate cDNA for SAGE library

construction can be employed except that a modified oligo-dT primer is used to derive the first strand synthesis. For example, the oligonucleotide of composition 5'-Biotin-TCC GGC GCG CCG TTT T CC CAG TCA $CGA_{(30)}$-3' (SEQ ID NO:208), contains a poly-T stretch at the 3' end for hybridization and priming from poly-A tails, an M13 priming site for use in subsequent PCR steps, a 5' Biotin label (B) for capture to strepavidin-coated magnetic beads, and an AscI restriction endonuclease site for releasing the cDNA from the streptavidin-coated magnetic beads. Theoretically, any sufficiently-sized DNA region capable of hybridizing to a PCR primer can be used as well as any other 8 base pair recognizing endonuclease.

cDNA constructed utilizing this or similar modified oligo-dT primer is then processed exactly as described in U.S. Patent No. 5,695,937 up until adapter ligation where only one adapter is ligated to the cDNA pool. After adapter ligation, the cDNA is released from the streptavidin-coated magnetic beads and is then used as a template for cDNA amplification.

Various PCR protocols can be employed using PCR priming sites within the 3' modified oligo-dT primer and the SAGE tag. The SAGE tag-derived PCR primer employed can be of varying length dictated by 5' extension of the tag into the adaptor sequence. cDNA products are now available for a variety of applications.

This technique can be further modified by: (1) altering the length and/or content of the modified oligo-dT primer; (2) ligating adaptors other than that previously employed within the SAGE protocol; (3) performing PCR from template retained on the streptavidin-coated magnetic beads; and (4) priming first strand cDNA synthesis with non-oligo-dT based primers.

3) *Isolation of cDNA using GeneTrapper or modified GeneTrapper Technology*

The reagents and manufacturer's instructions for this technology are commercially available from Life Technologies, Inc., Gaithersburg, Maryland.

Briefly a complex population of single-stranded phagemid DNA containing directional cDNA inserts is enriched for the target sequence by hybridization in solution to a biotinylated oligonucleotide probe complementary to the target sequence. The target sequence is based on the tag sequence of the present invention. The hybrids are captured on streptavidin-coated paramagnetic beads. A magnet retrieves the paramagnetic beads from the solution, leaving nonhybridized single-stranded DNAs behind. Subsequently, the captured single-stranded DNA target is released from the biotinylated oligonucleotide. After release, the cDNA clone is further enriched by using a nonbiotinylated target oligonucleotide to specifically prime conversion of the single-stranded target to double-stranded DNA. Following transformation and plating, typically 20% to 100% of the colonies represent the cDNA clone of interest. To identify the desired cDNA clone, the colonies may be screened by colony hybridization using the ^{32}P-labeled oligonucleotide as described above for solution hybridization, or alternatively by DNA sequencing and alignment of all sequences obtained from numerous clones to determine a consensus sequence.

4) Isolation of cDNAs from a library by probing with the SAGE transcript or tag

Classical methods of constructing cDNA libraries are taught in Sambrook et al., *supra*. Recent procedures described in Velculescu et al. (1997) Science 270:484) can be employed to construct an expression cDNA library cloned into the ZAP Express vector. A ZAP Express cDNA synthesis kit is available from Stratagene is used accordingly to the manufacturer's protocol. Plates containing 250 to 2000 plaques are hybridized as described in Rupert et al. (1988) Mol. Cell. Bio. 8:3104 to oligomucleotide probes with the same conditions previously described for standard probes except that the hybridization temperature is reduced to room temperature. Washes are performed in 6X standard-saline-citrate 0.1% SDS for 30 minutes at room temperature. The probes are labeled with ^{32}P-ATP through use of T4 polynucleotide kinase.

5) Identification of known genes or ESTs

In addition, databases exist that reduce the complexity of ESTs by assembling contiguous EST sequences into tentative genes. For example, TIGR has assembled human ESTs into a database called THC for tentative human consensus sequences. The THC database allows for a more definitive assignment compared to ESTs alone. Software programs exist (TIGR assembler and TIGEM EST assembly machine and contig assembly program (see Huang, X. (1996) Genomics 33:21-23)) that allow for assembling ESTs into contiguous sequences from any organism.

Isolation, culturing and expansion of APCs including Dendritic cells

Various methods to isolate and characterize APCs including DCs have been known in the art. At least two methods have been used for the generation of human dendritic cells from hematopoietic precursor cells in peripheral blood or bone marrow. One approach cultures the monocytes in GM-CSF and IL-4 as described below, where the immature portion was used for SAGE while an additional portion was treated with TNF-α for 36 hours to encourage their maturation. This method was followed for the isolation and culturing of the cell line identified herein as TNF-α matured dendritic cells.

The other method makes use of the more abundant CD34 precursor population, such as adherent peripheral blood monocytes, and stimulate them with GM-CSF plus IL-4 (see, for example, Sallusto et al. (1994), *supra).*

In other aspects of the invention, the methods described in Romani et al. (1996), *supra* or Bender et al. (1996), *supra* are used to generate both immature and mature dendritic cells from the peripheral blood mononuclear cells (PBMC) of a mammal, such as a murine, simian or human. Briefly, isolated PBMC are pre-treated to deplete T- and B-cells by means of an immunomagnetic technique. Lymphocyte-depleted PBMC are then cultured for 7 days in RPMI medium, supplemented with 1% autologous human plasma and GM-CSF/IL-4, to generate dendritic cells. On day 7, non-adherent cells are harvested for further processing.

The dendritic cells derived from PBMC in the presence of GM-CSF and IL-4 are immature, in that they can lose den Iritic cell properties and revert back to macrophage cell fate if the cytokine stimuli are removed from the culture. A population of dendritic cells having these features were used to isolate the transcripts of immature dendritic cells. The dendritic cells in an immature state are very effective in processing native protein antigens for the MHC class II restricted pathway (Romani et al. (1989) J. Exp. Med 169:1169.)

Further maturation is accomplished by culturing in conditioned medium or treating with LPS or TNF-α or CD40 ligand for 3 days in a macrophage-conditioned medium (CM), which contains the necessary maturation factors. Mature dendritic cells are less able to capture new proteins for presentation but are much better at stimulating resting T cells (both $CD4^+$ and $CD8^-$) to grow and differentiate.

Mature dendritic cells can be identified by their change in morphology, such as the formation of more motile cytoplasmic processes; by the presence of at least one of the following markers: CD83, CD68, HLA-DR or CD86; or by the loss of Fc receptors such as CD115 (reviewed in Steinman (1991) Ann. Rev. Immunol. 9:271.)

Computational Analysis

This tags identified and claimed herein and populations thereof can be used in further computational analysis. The sequences and expression profiles of this invention are stored in any functionally relevant program, e.g., in Compare Report using the SAGE software (available through Dr. Ken Kinzler at Johns Hopkins University). The Compare Report provides a tabulation of the polynucleotide sequences and their abundance for the samples normalized to a defined number of polynucleotides per library (say 25,000). This information can be imported into MS-ACCESS either directly or via copying the data into an Excel spreadsheet first and then from there into MS-ACCESS for additional manipulations. Other programs such as SYBASE or Oracle that permit the

comparison of polynucleotide numbers could be used as alternatives to MS-ACCESS. Enhancements to the software can be designed to incorporate these additional functions. These functions consist in standard Boolean, algebraic, and text search operations, applied in various combinations to reduce a large input set of polynucleotides to a manageable subset of polynucleotides of specifically defined interest.

Sequence information and abundance from a test sample or cell also is input into the functionally relevant program.

The researcher may create groups containing one or more project(s) by combining the counts of specific polynucleotides within a group (e.g., GroupNormal = Normal1 + Normal2, GroupTumor = PrimaryTumor1 + TumorCellLine). Additional characteristic values are also calculated for each tag in the group (e.g., average count, minimum count, maximum count). The researcher may calculate individual tag count ratios between groups, for example the ratio of the average GroupNormal count to the average GroupTumor count for each polynucleotide. The researcher may calculate a statistical measure of the significance of observed differences in tag counts between groups.

To identify the polynucleotides within MS-ACCESS, a query to sort polynucleotide tags based on their abundance in the sample cells is run. The output from the Query report lists specific polynucleotides (by sequence) that fit the sorting criteria and their abundance in the various sample cells.

The sorting is based on the principle that the gene product of interest (and hence the corresponding polynucleotide) is more abundant in the samples that prominently exhibit the chosen phenotype than in samples that do not exhibit the phenotype.

For example, one may query to identify polynucleotides that are present at a level of 10 tags when the total number of tags per library has been normalized to a defined number in the reference sample against one or more test samples. The results of the search might reveal that 5 different polynucleotides fit the sorting criteria, hence there are 5 candidates genes to be tested to determine whether they

confer the phenotype when transferred into samples that do not have the phenotype.

The more stringent the sorting criteria, the more efficient the sorting should be. Thus if one asked for polynucleotides that are at 5 tags when the total number of tags per library has been normalized to a defined number in the reference sample and less than 5 in the test sample, a large number of candidates would be generated. However, if one can increase the differential because the samples manifest extremes of the phenotype (say >10 in the test sample and <1 in the one or more reference samples) this restricts the number of candidates that will be identified.

Prior knowledge of what amount of gene product (hence abundance of polynucleotides) is required to confer the phenotype is not essential as one can arbitrarily select a set of sorting parameters, run the data analysis, and identify and test candidates. If the desired candidate is not found the stringency of the sorting criteria can be reduced (i.e. reduce the differential) and the new candidates that are found can be tested. Iterative cycles of sorting and testing candidates should eventually culminate in the successful recovery of the desired candidate.

Knowledge of what amount of gene product (hence abundance of polynucleotide) is required to confer the phenotype will permit the rationale use of stringent sorting criteria and greatly accelerate the search process as the desired gene may be captured within a handful of candidates

Establishing what amount of gene product is required to confer a specific phenotype will be dependent on the specific phenotype in question and the sensitivity of assays that measure that phenotype.

Accordingly, one enters the individual polynucleotide sequences from the Query report into the program to determine if there is a match with any known genes or whether they are potentially novel (no match=NM).

One then retrieves cDNAs corresponding to specific sequences from the Query Report and test them individually in an appropriate biological assay to determine if they confer the phenotype. Of the candidates that correspond to

known genes, it is a relatively easy task to obtain complementary DNAs for these candidates and test them individually to determine if they confer the specific phenotype in question when transferred into cells that do not exhibit the phenotype. If none of the known genes confer the phenotype, retrieve the cDNAs corresponding to the No Match sequences of the Query Report by PCR cloning and test the novel cDNAs individually for their ability to confer the phenotype. If the assumptions made up to this point are sound (i.e., a single gene product can confer the phenotype; the sorting criteria are not too stringent so as to exclude the desired candidate) then a cDNA corresponding to one of the candidates of the Query Report will be found to confer the phenotype and the search is over. If however none of the candidates are found to confer the phenotype then one may need to reduce the stringency of the sorting parameters to "cast a wider net" and capture more candidates to be tested as above.

In one embodiment, the polynucleotide or gene sequence can also be compared to a sequence database, for example, using a computer method to match a sample sequence with known sequences. Sequence identity can be determined by a sequence comparison using, i.e., sequence alignment programs that are known in the art, such as those described in CURRENT PROTOCOLS IN MOLECULAR BIOLOGY (F.M. Ausubel et al., eds., 1987) Supplement 30, section 7.7.18, Table 7.7.1. A preferred alignment program is ALIGN Plus (Scientific and Educational Software, Pennsylvania), preferably using default parameters, which are as follows: mismatch = 2; open gap = 0; and extend gap = 2. Another preferred program is the BLAST program for alignment of two nucleotide sequences, using default parameters as follows: open gap = 50; extension gap - 2 penalties; gap x dropoff = 0; expect = 10; word size = 11. The BLAST program is available at the following Internet address: http://www.ncbi.nlm.nih.gov. Alternatively, hybridization under conditions of high, moderate and low stringency can also indicate degree of sequence identity.

Vaccines for Cancer Treatment and Prevention

In one embodiment, the present invention comprises vaccines for cancer treatment. Recent advances in vaccine adjuvants provide effective means of administering peptides so that they impact maximally on the immune system. Del-Giudice (1994) Experientia 50:1061-1066. A polynucleotide of this invention can be administered in alone or in combination with a polynucleotide encoding an antigenic peptide as a cancer vaccine. The polynucleotide can be administered as naked DNA or alternatively, in expression vectors. Therapy can be enhanced by coadministration of cytokine and/or co-stimulatory molecules which in turn, can be administered as proteins or the polynucleotides encoding the proteins.

Host cells comprising Antigenic Peptides of the Invention

The invention further provides isolated host cells comprising the polynucleotide of the invention. In some embodiments, these host cells present one or more peptides of the invention on the surface of the cell in the context of an MHC molecule, i.e., a antigenic peptide of the invention is bound to a cell surface MHC molecule such that the peptide can be recognized by an immune effector cell. Isolated host cells which present the polypeptides of this invention in the context of MHC molecules are further useful to expand and isolate a population of educated, antigen-specific immune effector cells. The immune effector cells, e.g., cytotoxic T lymphocytes, are produced by culturing naïve immune effector cells with antigen-presenting cells cells which present the polypeptides in the context of MHC molecules on the surface of the APCs. The population can be purified using methods known in the art, e.g., FACS analysis or FICOL™ gradient. The methods to generate and culture the immune effector cells as well as the populations produced thereby also are the inventors' contribution and invention. Pharmaceutical compositions comprising the cells and pharmaceutically acceptable carriers are useful in adoptive immunotherapy. Prior to administration *in vivo*, the immune effector cells are screened *in vitro* for their ability to lyse melanoma tumor cells.

Gene transfer

Vectors useful in genetic modification

In one embodiment, the present invention provides methods of eliciting efficient antigen-specific immune response in a subject by introducing to the subject recombinant polynucleotides encoding antigenic peptides alone or in combination with immunostimulatory factors. Methods and materials for gene transfer are known in the art, including, for example, viral mediated gene transfer, lipofection, transformation, transfection and transduction. The polynucleotides encoding the immunostimulatory factor and target antigenic peptide can be introduced ex vivo into a host cell, for example, dendritic cells. The genetically modified host cells can be introduced as a cell-based vaccine into the target subject. Alternatively, the polynucleotides encoding the immunostimulatory factor and target antigenic peptide can be introduced directly into the subject in the form of gene-based vaccine.

Various viral infection techniques have been developed which utilize recombinant viral vectors for gene delivery, and constitute preferred approaches to the present invention. The viral vectors which have been used in gene transfer include, but not limited to, viral sequences derived from simian virus 40 (SV40), adenovirus, adeno-associated virus (AAV), and retroviruses.

Vector Transduction of Cells such as APCs

APCs can be transduced with viral vectors encoding a relevant polypeptides. The most common viral vectors include recombinant poxviruses such as vaccinia and fowlpox virus (Bronte et al. (1997) Proc. Natl. Acad. Sci. USA **94**:3183-3188; Kim et al. (1997) J. Immunother. **20**:276-286) and, preferentially, adenovirus (Arthur et al. (1997) J. Immunol. **159**:1393-1403; Wan et al. (1997) Human Gene Therapy **8**:1355-1363; Huang et al. (1995) J. Virol. **69**:2257-2263). Retrovirus also may be used for transduction of human APCs (Marin et al. (1996) J. Virol. **70**:2957-2962).

In vitro or *ex vivo* exposure of human DCs to adenovirus (Ad) vector at a multiplicity of infection (MOI) of 500 for 16-24 h in a minimal volume of serum-free medium reliably gives rise to foreign polynucleotide expression in 90-100% of DCs. The efficiency of transduction of DCs or other APCs can be assessed by immunofluorescence using fluorescent antibodies specific for the tumor antigen being expressed (Kim et al. (1997) J. Immunother. **20**:276-286). Alternatively, the antibodies can be conjugated to an enzyme (e.g. HRP) giving rise to a colored product upon reaction with the substrate. The actual amount of antigenic polypeptides being expressed by the APCs can be evaluated by ELISA.

In vivo transduction of DCs, or other APCs, can be accomplished by administration of Ad (or other viral vectors) via different routes including intravenous, intramuscular, intranasal, intraperitoneal or cutaneous delivery. The preferred method is cutaneous delivery of Ad vector at multiple sites using a total dose of approximately $1x10^{10}$-$1x\ 10^{12}$ i.u. Levels of *in vivo* transduction can be roughly assessed by co-staining with antibodies directed against APC marker(s) and the antigen being expressed. The staining procedure can be carried out on biopsy samples from the site of administration or on cells from draining lymph nodes or other organs where APCs (in particular DCs) may have migrated (Condon et al. (1996) Nature Med. **2**:1122-1128; Wan et al. (1997) Human Gene Therapy **8**:1355-1363). The amount of antigen being expressed at the site of injection or in other organs where transduced APCs may have migrated can be evaluated by ELISA on tissue homogenates.

Although viral gene delivery is more efficient, DCs can also be transduced *in vitro/ex vivo* by non-viral gene delivery methods such as electroporation, calcium phosphate precipitation or cationic lipid/plasmid DNA complexes (Arthur et al. (1997) Cancer Gene Therapy **4**:17-25). Transduced APCs can subsequently be administered to the host via an intravenous. Subcutaneous, intranasal, intramuscular or intraperitoneal route of delivery.

In vivo transduction of DCs, or other APCs, can potentially be accomplished by administration of cationic lipid/plasl lid DNA complexes

delivered via the intravenous, intramuscular, intranasal, intraperitoneal or cutaneous route of administration. Gene gun delivery or injection of naked plasmid DNA into the skin also leads to transduction of DCs (Condon et al. (1996) Nature Med. 2:1122-1128 and Raz et al. (1994) Proc. Natl. Acad. Sci. USA 91:9519-9523). Intramuscular delivery of plasmid DNA may also be used for immunization (Rosato et al. (1997) Human Gene Therapy 8:1451-1458.

The transduction efficiency and levels of foreign polynucleotide expression can be assessed as described above for viral vectors.

Administration of Cell-Based Vaccine to Subject

Genetically modified cells can subsequently be administered to the host subject via various routes, including, for example, intravenous infusion, subcutaneous injection, intranasal, intramuscular or intraperitoneal delivery. The cells containing the recombinant polynucleotides may be used to confer immunity to individuals. Administration *in vivo* can be effected in one dose, continuously or intermittently throughout the course of treatment. Methods of determining the most effective means and dosage of administration are well known to those of skill in the art and will vary with the composition used for therapy, the purpose of the therapy, the target cell being treated, and the subject being treated. Single or multiple administrations can be carried out with the dose level and pattern being selected by the treating physician.

Adoptive Immunotherapy Methods

The expanded populations of antigen-specific immune effector cells and APCs presenting antigens find use in adoptive immunotherapy regimes.

Adoptive immunotherapy methods involve, in one aspect, administering to a subject a substantially pure population of educated, antigen-specific immune effector cells made by culturing naïve immune effector cells with APCs as described above. In some embodiments, the APCs are dendritic cells.

In one embodiment, the adoptive immunotherapy methods described herein are autologous. In this case, the APCs are made using parental cells isolated from a single subject. The expanded population also employs T cells isolated from that subject. Finally, the expanded population of antigen-specific cells is administered tothe same patient.

In a further embodiment, APCs or immune effector cells are administered with an effective amount of a stimulatory cytokine, such as IL-2 or a co-stimulatory molecule.

Immune Effector Cells

The present invention makes use of the above-described antigen-presenting matrices, including APCs, to stimulate production of an enriched population of antigen-specific immune effector cells. Accordingly, the present invention provides a population of cells enriched in educated, antigen-specific immune effector cells, specific for an antigenic peptide of the invention. These cells can cross-react with (bind specifically to) antigenic determinants (epitopes) on natural (endogenous) antigens. In some embodiments, the natural antigen is on the surface of tumor cells and the educated, antigen-specific immune effector cells of the invention suppress growth of the tumor cells. When APCs are used, the antigen-specific immune effector cells are expanded at the expense of the APCs, which die in the culture. The process by which naïve immune effector cells become educated by other cells is described essentially in Coulie (1997) Molec. Med. Today 3:261-268.

An effector cell population suitable for use in the methods of the present invention can be autogeneic or allogeneic, preferably autogeneic. When effector cells are allogeneic, preferably the cells are depleted of alloreactive cells before use. This can be accomplished by any known means, including, for example, by mixing the allogeneic effector cells and a recipient cell population and incubating them for a suitable time, then depleting CD69$^+$ cells, or inactivating alloreactive cells, or inducing anergy in the alloreactive cell population.

Hybrid immune effector cells can also be used. Immune effector cell hybrids are known in the art and have been described in various publications. See, for example, International Patent Application Nos. WO 98/46785; and WO 95/16775.

Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it will be apparent to those skilled in the art that certain changes and modifications will be practiced. Therefore, the description and examples should not be construed as limiting the scope of the invention, which is delineated by the appended claims.

Example 1

The Table illustrates a series of mRNAs, both known and unknown, that were found by SAGE analysis to be differentially expressed in monocyte-derived dendritic cells as compared to monocytes. SAGE analysis revealed for instance that the chemokines PARC and TARC that can recruit activated T cells are differentially expressed by monocyte-derived immature dendritic cells (prepared by culturing PBMC derived monocytes in GM-CSF and IL4). Other immunostimulatory factors to mention include: monocyte chemotactic protein-4 (MCP-4) [Berkhout et al., (1997) Journal of Biological Chemistry 272(26): 16404-16413] U46767; macrophage-derived chemokine (MDC) [Godiska et al., (1997) Journal of Experimental Medicine 185(9): 1595-1604] U83171; ecalectin [Matsumoto et al., (1998) Journal of Biological Chemistry 273(27): 16976-16984], AB005894; and monocyte chemotactic protein-2 (MCP-2) [Proost et al., 1996 Journla of Leukocyte Biology 59(1): 67-74] Y10802. The fact that dendritic cells produce abundant levels of these chemokines has not been reported previously. The genes encoding these chemokines could be linked to the gene or genes encoding tumor antigens in a DNA based vaccine to ensure that APCs transduced with the vaccine will produce and process not only the tumor antigen, but also the stimulatory chemokines. Any cDNA or gene encoding any of the mRNAs or combination of mRNAs identified by differential gene expression

analysis (such as SAGE) as being differentially expressed in immature dendritic cells as shown in Table I could be linked to a tumor antigen gene or genes to prepare superior vaccines. Similarly, any cDNA or gene encoding any mRNA or combination of mRNAs identified by differential gene expression analysis (such as SAGE) as being differentially expressed in mature dendritic cells could be linked to a tumor antigen gene or genes to prepare superior vaccines.

Example 2

The genes encoding mRNAs that are differentially expressed in either immature or mature dendritic cells are apt to be regulated by specific transcription factors. Thus, an alternative to delivering the gene encoding an mRNA identified as being differentially expressed in either mature or immature dendritic cells by comparative gene expression analysis (such as SAGE) would be to deliver a gene or genes that encode transcription factors (either naturally occurring or engineered via recombinant DNA technology) that can transactivate the expression of the endogenous gene that encodes the differentially expressed mRNA. Thus, the present invention also pertains to vaccines in which a gene or genes encoding tumor antigens is linked to genes encoding transcription factors or transactivators that can upregulate the expression of mRNAs identified as being differentially expressed in either mature or immature dendritic cells by comparative gene expression analysis.

Example 3

Differential gene expression analysis would also be expected to reveal genes encoding cell surface proteins that are preferentially expressed by either immature or mature dendritic cells as compared to monocyte precursors. These cell surface molecules may play a pivotal role in the function of dendritic cells by acting as co-stimulatory signals or modulators of DC function or migration. Naturally occurring ligands specific for these cell surface molecules or recombinant proteins (such as an antibody) generated to have specificity for these

cell surface molecules might be expected to interact with the cell surface protein to stimulate the function of the dendritic cells or foster the maintenance of an activated state or stimulate the migration of dendritic cells to sites rich in T cells. Thus, the present invention relates to vaccines in which a gene or genes encoding tumor antigen or antigens is linked to a gene or genes encoding secreted proteins that have the capacity to bind to and modulate the activity of cell surface proteins identified as being differentially expressed in either mature or immature dendritic cells by comparative gene expression analysis (such as SAGE). In this manner, a novel autocrine loop is established whereby a genetically modified APC produces a ligand that is secreted from the APC where it can bind to cell surface receptors on that cell and stimulate the genetically modified dendritic cell.

Although the foregoing invention has been described in some detail by way of illustration and example for purposes of clarity of understanding, it will be apparent to those skilled in the art that certain changes and modifications will be practiced. Therefore, the description and examples should not be construed as limiting the scope of the invention, which is delineated by the appended claims.

TABLE 1

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TATATTTTCT	1.	Human transglutaminase mRNA, 3' untranslated region.	M98479
TCTCCATACC	2.	mitochondrial	
AGAAGTGTCC	3.	Homo sapiens (HepG2) LAL mRNA for lysosomal acid lipase.	Z31690
GGCACAAAGG	4.	Human mRNA for chemokine, complete cds.	D43767
TGGCCCCAGG	5.	Human mRNA for precursor of apolipoprotein CI (apo CI).	X00570
TGTACCTGTA	6.	Homo sapiens (xs31) mRNA, 835bp.	Z36832
AAGGGATGCT	7.	Human monocyte chemoattractant protein-4 precursor (MCP-4) mRNA,	U46767
GAGGGTGCCA	8.	Human complement component 1, beta-chain (C1QB) mRNA, partial cds.	M36278
TCTTGATTTA	9.	Human alpha-2-macroglobulin mRNA, complete cds.	M11313
CGACCCCACG	10.	Human apolipoprotein E mRNA, complete cds.	M12529
ACCCGCCGGG	11.	18s ribosomal RNA	
ATCTTGTTAC	12.	Human mRNA for fibronectin (FN precursor).	X02761 K00
GGGGGTGAAG	13.	Homo sapiens mRNA for CCAAT/enhancer binding protein alpha.	Y11525
CCTTGTCCTC	14.	Homo sapiens mRNA for GM2 activator protein.	X62078
GCCGCTACTT	15.	Homo sapiens mRNA encoding RAMP1.	AJ001014
CTGGGCCTGG	16.	Hs.74573: Human HU-K4 mRNA, complete cds H	
GACCCGCTGG	17.	xxx	
ATATACTGTG	18.	AC005102 Homo sapiens clone RG356E01, complete seq	
AAACTTTGCC	19.		
ACTATTTCCA	20.	Human long transcript fructose-1,6-bisphosphatase (HUMFBPase) mRNA,	U47918
ACCCAGGGTA	21.	Hs.153876: ESTs Hs.153876: ESTsHs.153876:	
ACTGGAACGA	22.	Homo sapiens NADP-dependent isocitrate dehydrogenase (IDH) mRNA,	AF020038

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
AACGGGGCCC	23.	Human macrophage-derived chemokine precursor (MDC) mRNA, complete	U83171
CCTGGGGTAA	24.	Human mRNA for DC classII histocompatibility antigen alpha-chain.	X00452 K01
TCACCGGTCA	25.	Human mRNA for plasma gelsolin.	X04412
AATGCAGGCA	26.	Human S-adenosylhomocysteine hydrolase (AHCY) mRNA, complete cds.	M61831
CTGACCTGTG	27.	Human heart mRNA for MHC class I HLA-Bw62, partial cds.	D87665
GATCAATCAG	28.	Homo sapiens mRNA for CC chemokine. complete cds.	AB000221
CCCCCTGCCC	29.		
GTGACCACGG	30.	Human N-methyl-D-aspartate receptor 2C subunit pre	
TGTCCCAGCC	31.	Human mRNA for acid phosphatase type 5 (EC 3.1.3.2).	X14618
ACCTTTACTG	32.		
GTGTGTAAAA	33.		
TGTTTGGGGG	34.		
AATATTGCAC	35.		
TGGCTGGCCA	36.		
GCGTCTGGGG	37.		
TATTTATTCC	38.	Human mRNA for Src-like adapter protein, complete cds.	D89077
CTGGGCCAGC	39.	ESTs, Weakly similar to SYNAPTOBREVIN 2 [Homo sapiens	
CTTGATTCCC	40.	Homo sapiens quiescin (Q6) mRNA. complete cds.	U97276
CTCATAAGGA	41.	Tag matches mitochondrial DNA	
AGAGGTGTAG	42.	xxx	
CCTCACTACC	43.	xxx	
AAGAAGCAGG	44.	Homo sapiens unknown mRNA, complete cds.	AF047439
TGGCTAGTGT	45.	Human mRNA for proteasome subunit z, complete cds.	D38048
CTCTAAGAAG	46.	Hs.9641: ESTs, Highly similar to COMPLEMENT C1Q SU	
TGGCTGTGTG	47.		
ATCCTCCCTA	48.		
TCCTACGTGA	49.		
TGGGAAACCT	50.		
GCGAAACCCA	51.	several hits	
AGTATCTGGG	52.	Homo sapiens Arp2/3 protein complex subunit p41-Arc (ARC41) mRNA.	AF006084

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
CCCTCGGTCC	53.		
GTAATCCTGC	54.		
TCGTAACGAG	55.		
ACTTAGGGAG	56.	Human MrNA for LIMK (LIM kinase). complete cds.	D26309
GAGGAAGAAG	57.	tumor rejection antigenendoplasmic reticular heat shock protein	S74942
TGGAAGGGCA	58.		
CTAGCCAGCA	59.		
TATTATTAAA	60.		
GCCATCCAGA	61.	Hs.107479: Homo sapiens mRNA for KIAA0738 protein,	
TATTGGCCTG	62.	Hs.79572: Cathepsin D (lysosomal aspartyl protease	
GCCACCCCGT	63.	Human mRNA for glucose-6-phosphate dehydrogenase (G6PD).	X03674
CGCCGACGAT	64.	Human interferon-inducible mRNA fragment (cDNA 6-16).	X02492 X02
GCTCTGCCTC	65.	Homo sapiens cathepsin X precursor, mRNA, complete cds.	AF073890
CCTGTACCCC	66.	Homo sapiens Sox-like transcriptional factor mRNA, complete cds.	AF072836
TGTCGCTGGG	67.	Hs.154811: C4/C2 activating component of Ra-reacti	
AGAAGCCGTG	68.	Human neutrophil adherence receptor alpha-M subunit mRNA.	J04145
GGAAAATGGG	69.	xxx	
GATACAGCCA	70.	Human mRNA for lymphocyte IgE receptor (low affinity receptor Fc	X04772
ATGTGCGTGG	71.	Human SNC19 mRNA sequence.	U20428
AAGGCGTTTC	72.		
GAGAACGGGG	73.		
CAGAATGACT	74.		
GGGAAACAGG	75.		
CTGTCTTGGG	76.		
GTCTGAGCTC	77.		
GTGGCTTCCC	78.		
TATCTGTCTA	79.		
TGCTTTGGGA	80.		
TCTCTGATGC	81.	Homo sapiens mRNA for SH3 binding protein, complete cds,	AB000462
AAATCAATAC	82.		
AGCCGGGATG	83.	Homo sapiens RING12 mRNA.	X62741
GCAGGCCATA	84.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
GGGCCCAGGA	85.		
TTGTCGATGG	86.	Homo sapiens full length insert cDNA clone ZE12H05.	AF086553
TGGGCTCTGA	87.	Human mRNA for lysosomal sialoglycoprotein, complete cds.	D12676
CAGTCATTTG	88.		
TTTCTAGTTT	89.	Human mRNA for KIAA0108 gene, complete cds.	D14696
TGGATCCTAG	90.	Homo sapiens NADH:ubiquinone oxidoreductase NDUFS3 subunit mRNA.	AF067139
TCTCCAGGAA	91.		
GCTTTGCAGT	92.	Homo sapiens TWIK-related acid-sensitive K+ channel (TASK) mRNA.	AF006823
AGTTTCCCAA	93.	Homo sapiens SULT1C sulfotransferase (SULT1C) mRNA, complete cds.	AF055584
TCCACGCACC	94.		
CACCGCTGCA	95.		
GTGATGGATG	96.		
AGTGTATTTT	97.	Human mRNA for insuline-like growth factor II receptor.	Y00285
AATGACTGAA	98.		
GGAGATGAGG	99.		
TTGAGACCTC	100.	Human factor XIII subunit a mRNA, 3' end.	M14539
CTACACCAGT	101.		
GCCGTTCTTA	102.	xxx	
TGCAGAAGAA	103.	Homo sapiens mRNA for macrophage mannose receptor.	X55635
CTAACTAGTT	104.	xxx	
GCCTGCAGTC	105.	Homo sapiens mRNA for hepatocyte growth factor activator inhibitor	AB006534
ACATTCTTTT	106.	Homo sapiens NMB mRNA.	X76534
TTTGTAGATG	107.	Human HepG2 3' region MboI cDNA. clone hmd3c06m3.	D17196
ACAACTCAAT	108.	Human HepG2 3' region cDNA, clone hmd4h10.	D16936
TCAGATAGGA	109.	Human MAPKAP kinase (3pK) mRNA, complete cds.	U09578
ATTAAGAGGG	110.		
GTGTGTCTGA	111.	Human mRNA encoding major histocompatibility complex gene HLA-DR	V00522
CAGCATCTAA	112.		
ATGTAGGTGC	113.	Homo sapiens mRNA for phosphatidic	AB000889

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
		acid phosphatase 2b, complete	
TGAGAGCAGC	114.		
TTTTAGCAGG	115.	Homo sapiens clone 24560 unknown mRNA, complete cds.	AF055001
GGTGAAGAGG	116.	Homo sapiens mRNA for hepatocyte growth factor activator inhibitor,	AB000095
GAAGTCGGAA	117.		
CTATATTTTT	118.	Homo sapiens mRNA for cathepsin C.	X87212
TCCTGCTGGC	119.		
GTCAGAATGG	120.	Homo sapiens clone 23863 mRNA, partial cds.	AF035299
GCAACGGGCC	121.	Homo sapiens mRNA for brain acyl-CoA hydrolase, complete cds.	D88894
CTGATCTCCA	122.		
AACTAATACT	123.		
AATGGATGAA	124.		
CACATCCTTA	125.		
CCACGCACTG	126.		
TAGGTCACCT	127.		
ATTTAGCAAG	128.		
CTGGATGGGC	129.		
TTGGAACAAT	130.		
CAGGATCCAG	131.	Human progesterone receptor-associated p48 protein mRNA, complete	U28918
GTGACTGCCA	132.	Homo sapiens clone 24722 unknown mRNA, partial cds.	AF055020
GCTTGCTGGC	133.		
CCCTGGGCGA	134.		
CCCCTCCCCC	135.	Human velo-cardio-facial syndrome 22q11 region mRNA sequence.	U84524
GATTACCTGT	136.		
TCAATAAATG	137.		
GGCCCTCTGA	138.	Human peptidyl-prolyl isomerase and essential mitotic regulator	U49070
ACCAGAGGGG	139.		
GACGTTCACT	140.		
TGGCAAACGT	141.		
CAAGACGGGG	142.		
CAGGTTGTGA	143.	Human mRNA for lysosomal acid phosphatase (EC 3.1.3.2).	X12548
CTTGACCTGT	144.		
TACCCCACCC	145.	Human zinc finger protein (MAZ) mRNA.	M94046

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TTACCTTTTT	146.	Human beta-D-galactosidase mRNA, complete cds.	M27507 J05
AGCAGCAACA	147.		
ACTATTAGTG	148.	Homo sapiens doc-1 mRNA, complete cds.	AB006077
ATTGCTCTCT	149.		
GCCCCAGCCC	150.	Human chitotriosidase precursor mRNA, complete cds.	U29615
GGTGGGGAGA	151.	Human chromosome 17q21 mRNA clone LF113.	U18009
ACCAGCCACA	152.	cysteine proteinase cystatin c	
TGCCTCTGCG	153.	Homo sapiens mRNA for CD151, complete cds.	D29963
ATATAATCTG	154.	Human non-integrin laminin-binding protein mRNA, complete cds.	M36682
GGAGCAGACG	155.		
GTGCGCTGAG	156.	Human mRNA for HLA class I locus C heavy chain.	X58536
TTTTCTGAAA	157.	Human thioredoxin (TXN) mRNA, complete cds.	J04026
CTGTTAGTGT	158.	Homo sapiens malate dehydrogenase (MDHA) mRNA, complete cds.	U20352
GAGGACTCCG	159.	Human tryptophanyl tRNA synthetase (IFNWRS) mRNA, complete cds.	M77804
GAAATACAGT	160.	Human cathepsin D mRNA, complete cds.	M11233
GGAACTTTTA	161.	Hs.43857: ESTs	
GAAGCAGGAC	162.	Homo sapiens mRNA for non-muscle type cofilin.	X95404
AGCCACCGCA	163.	Human mRNA upregulated during camptothecin-induced apoptosis of	U58668
ATGAAACTTC	164.	mitochondrial	
CTGGACCCGG	165.	Fructose 1-6 biphosphate	
GTGCTATTCT	166.		
AGGGCAGGGA	167.	Homo sapiens clone 24444 RaP2 interacting protein 8 (RPIP8) mRNA,	AF055026
GGCAGCGCCC	168.		
GCAGTTCTGA	169.	Human mRNA fragment for class II histocompatibility antigen	X00700
TCCTGGGTTC	170.		
GGTAGAACTA	171.		
AGCTCCCAGA	172.	Homo sapiens mRNA for ferritin L-chain.	Y09188
TCCTTACTAG	173.	Homo sapiens mRNA for GAIP protein.	X91809
GGCCTCTCCG	174.	Human membrane-associated protein	M58285

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
		(HEM-1) mRNA, complete cds.	
ACTCAGAAGA	175.		
CCCAAGCTAG	176.	Human clone 23827 heat shock protein mRNA, complete cds.	U90906
CAAAATGCAA	177.		
GGTGGATGTG	178.		
TGAGAGGAGA	179.	Homo sapiens NADH-ubiquinone oxidoreductase subunit CI-SGDH mRNA,	AF047181
AGAACAAAAC	180.	Homo sapiens mRNA for proliferation-associated gene (pag).	X67951
AGAACCTTAA	181.		
CAAATGCTGT	182.	Homo sapiens transcription factor ISGF-3 mRNA, complete cds.	M97935
CCCAGATGAT	183.		
CCTGTGTGTG	184.		
TGAGTCTGGC	185.		
CTTTTCTCTT	186.		
AGCAGCTGCT	187.	Homo sapiens HYL tyrosine kinase mRNA.	X77278
CCGGGTGATG	188.		
TCAAAAAAAA	189.		
CTGTGATTGT	190.	Homo sapiens FLAME-1 mRNA, complete cds.	AF009616
AATTGCAAGC	191.	Human cofilin mRNA.	D00682
AAAAATAAAG	192.	Homo sapiens mRNA for mitochondrial ATP synthase.	X65460
AACTGCTTCA	193.	Hs.11538: Homo sapiens Arp2/3 protein complex subu	
GACCACGAAT	194.	Human mRNA for cathepsin H (E.C.3.4.22.16.).	X07549
GAGAACGCAG	195.		
AGGACACCGC	196.	Human mRNA for C-SRC-kinase.	X59932 X71
TGGGTCATTT	197.		
GGGCAGAATT	198.	Human mRNA for KIAA0370 gene, partial cds.	AB002368
GGGCAAGCCA	199.	Human mRNA for steroid hormone receptor hERR1.	X51416 Y00
GCCAAGGGCC	200.		
CTGCTAGGGG	201.		
ACTCCTTCCT	202.		
CTTTTATGTA	203.		
CAGATTGTGA	204.		
CGCCCGTCGT	205.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
ACTAACTGTG	206.	Homo sapiens IEF 9306 mRNA.	X71810
GAATTTTATA	207.	Human peripheral benzodiazepine receptor related mRNA sequence.	L21950
ATGATGCGGT	208.	Homo sapiens thrombin inhibitor mRNA.	Z22658
GGAAGACATC	209.		
GGCAGTAGGC	210.		
AATGAATGAA	211.		
TAAATCTATA	212.	Homo sapiens hFcRII-C isoform mRNA for IgG Fc receptor hFcRII.	X17653
TTTACAGACC	213.	Homo sapiens clone 23953 mRNA sequence.	AF052111
CTTTCAGATG	214.	Human mRNA for platelet-type phosphofructokinase, complete cds.	D25328
GCGTGATCCT	215.	Human aldehyde reductase mRNA, complete cds.	J04794
CCCTCCTGGG	216.		
GTGTCGGGGG	217.		
GGGGTAAGAA	218.	Human mRNA for human homologue of rat phosphatidylethanolamine	D16111
TAAACTGTTT	219.		
GCCCCCCCGT	220.		
TTGGGCACTA	221.		
GCTGGGGTGG	222.	Homo sapiens mRNA for mediator of receptor-induced toxicity.	X84709
TGCTACTGGT	223.	Homo sapiens mRNA for SURF-1.	Z35093
AGAGGTGGTG	224.		
CGGTTACTGT	225.		
TTCTGAAGCA	226.		
CAGTTTGTAC	227.	Human mRNA for brain pyruvate dehydrogenase (EC 1.2.4.1).	X52709
ATGTGAAGAA	228.		
TCTGAAAACC	229.		
TTAACAAACT	230.		
TTATTGTTGC	231.		
GAAGTTTTAC	232.		
GTCATTATGC	233.		
TCTGGGAACA	234.	Human clone 23828 mRNA sequence.	U79285
CAGTGGGTGT	235.	Homo sapiens clone 24733 mRNA sequence.	AF052149
GGTTCTGTGT	236.		
CCCTCTGTCA	237.		
CCCTGGGTTC	238.	Human ferritin L chain mRNA, complete cds.	M11147
TGGGTGAGCC	239.	Human cathepsin B proteinase mRNA.	M14221

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
		complete cds.	
CCGACGGGCG	240.		
CACCACGGTG	241.		
ATTTCAGAAG	242.	Homo sapiens cellular repressor of E1A-stimulated genes CREG mRNA.	AF084523
TCCGCGAGAA	243.		
GGGTGCTTGG	244.		
GACCAGAAAA	245.	Human COX VIa-L mRNA for cytochrome c oxidase liver-specific	X15341
GCATCCCTCC	246.		
GAAGATGTGG	247.		
TTAGTTACCT	248.		
TCATTGTAAT	249.		
CAGCGCGCCC	250.		
CCTGTGATCC	251.		
CGTGGGTGGG	252.	Human mRNA for heme oxygenase.	X06985
ACATCGTAGG	253.		
CCTGGAAGAG	254.	Human thyroid hormone binding protein (p55) mRNA, complete cds.	J02783
GAAAAATGGT	255.	Homo sapiens mRNA for laminin-binding protein.	X61156
CTCAACCCCC	256.	Human mRNA for LDL-receptor related protein.	X13916
TAACCAATCA	257.	Human Rab5c-like protein mRNA, complete cds.	U11293
CTCAGTCCCC	258.	Homo sapiens mRNA for ecalectin, complete cds.	AB005894
CCCTGTAATA	259.		
TGGCGTACGG	260.		
CTGGCTGCAA	261.	Human cytochrome c oxidase subunit Vb (coxVb) mRNA, complete cds.	M19961
TGCTTGGGCA	262.	Human saposin proteins A-D mRNA, complete cds.	M32221
ACAGCAGCTT	263.	Homo sapiens mRNA for monocyte chemoattractant protein 4.	X98306
CCCTGGGGTT	264.		
CCAATCCTGA	265.		
TTCTTGCTTA	266.		
CCCTTAGCAA	267.		
ATAGGTAGAG	268.		
GCTGCTCCCT	269.		
GTGATCTCCG	270.		
AAGATTGGTG	271.	Homo sapiens mRNA for MRP-1.	X60111
ATGTGAAGAG	272.	Human SPARC/osteonectin mRNA,	J03040

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
		complete cds.	
CGCTGTGGGG	273.		
ACACAGCAAG	274.		
CTCAGACAGT	275.		
CCTGGGTTCT	276.		
TGGGGTGAGC	277.		
ACTATGACAA	278.		
TGGACACAAG	279.		
AGACTGATCC	280.	Homo sapiens mRNA for protein tyrosin kinase.	X73568
CAATATTACA	281.		
CCACACCGGT	282.	Human mRNA for heme oxygenase-2, complete cds.	D21243
ATAGGTCAGA	283.		
CCATCCGCAT	284.	Human lysosomal proteinase cathepsin B mRNA, 3' end.	M13230
TTTCCCCGCA	285.		
CTTCTATGTA	286.	Human mRNA for KIAA0177 gene, partial cds.	D79999
GCCCTGCTGA	287.		
GCGTCGGGGA	288.	Homo sapiens mRNA for soluble IFN alpha/beta receptor.	X89814
GGCAGAGGAC	289.	Human mRNA for Nm23 protein, involved in developmental regulation	X17620
CCAGTAATCC	290.		
TACACTACTG	291.		
TCTGGTCTGG	292.	Human surface antigen mRNA, complete cds.	M60922
CTTCTACTAA	293.		
TGGCACAAAC	294.		
TAGGCAACAC	295.		
GCACCTTCTG	296.		
GCCACTACCC	297.		
GACCCACCTT	298.		
CGCTGTGTGC	299.	Human mRNA for glucocerebrosidase, complete cds.	D13286
GATCTTTTGT	300.	Homo sapiens mRNA for Fln29, complete cds.	AB007447
TCACTGAGTT	301.		
ATTGTGCTTG	302.		
TGTAAGGCAC	303.		
TGAACCTCTG	304.	Homo sapiens Ca2+-dependent phospholipase A2 mRNA, complete cds.	U03090

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
CGGATAACCA	305.	Human cell cycle protein p38-2G4 homolog (hG4-1) mRNA, complete	U59435
GTTCAGCTGT	306.	Homo sapiens porin (por) mRNA, complete cds and truncated cds.	L08666
AAAAAACCCA	307.		
ATAGACATAA	308.	Human pre-mRNA splicing factor SF2p32, complete sequence.	M69039
CTCATAAGAA	309.		
CTGAGCACAA	310.		
TTTTGTGTGA	311.		
TTTTCCTGCA	312.		
AGTATGTATG	313.		
GCTGTCATCA	314.	Human 26S protease (S4) regulatory subunit mRNA, complete cds.	L02426
GACTGTGCCA	315.	Human cytoplasmic dynein light chain 1 (hdlc1) mRNA, complete cds.	U32944
TCACAAAAGA	316.	Homo sapiens chromosome 11 beta-1,4-galactosyltransferase mRNA,	AF038663
TTGCTGGAGA	317.		
GTCAAGACCA	318.	Human beta adaptin protein mRNA, complete cds.	L13939
GGAGGTGGGG	319.	Homo sapiens clone 24720 epithelin 1 and 2 mRNA, complete cds.	AF055008
GTGCAAAATG	320.		
GTGGGGGGAG	321.		
ACCCCAGCAA	322.		
CAATGTGAGC	323.		
CATTGTATTA	324.		
GCTTCCATCT	325.	Homo sapiens BAT1 mRNA for nuclear RNA helicase (DEAD family).	Z37166
ATGGGTTTGC	326.		
CCCAATAAAC	327.		
CCCTGGGCTC	328.		
CTGCGGTGGC	329.		
CATCTAAACT	330.	Human mRNA for KIAA0038 gene, partial cds.	D26068
TGTTTATCCT	331.	Human diazepam binding inhibitor (DBI) mRNA, complete cds.	M14200
ACCTCAATTA	332.	Human ALAS1 (ALASH) mRNA for delta-aminolevulinate synthase	X56351
ACTCAGGTGA	333.		
ACTTGAGCTT	334.	Homo sapiens mRNA for cystinosin.	AJ222967
AGGCTACGGG	335.		
GGAAGAGAAG	336.	Homo sapiens mRNA for Rer1 protein.	AJ001421

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TTTTATTAAA	337.		
ATACTGTCAG	338.		
CTTCTGCTGG	339.	Homo sapiens retinal short-chain dehydrogenase/reductase retSDR1	AF061741
TTACGAGGAA	340.	Homo sapiens clone 24761 mRNA sequence.	AF052155
AATCCAGGAG	341.		
TGGGCCTGTG	342.		
ATAGTAGCTT	343.	Human actin bundling protein (HSN) mRNA, complete cds.	U03057
TGGAAGGACC	344.		
AATAGAAATT	345.	Homo sapiens clone 23810 osteopontin mRNA, complete cds.	AF052124
TTGAGCCAGC	346.	Human KH type splicing regulatory protein KSRP mRNA, complete cds.	U94832
TTGGCCAGGT	347.		
TACTGTGATG	348.		
ATCTTGAAAG	349.	Homo sapiens NAP (nucleosome assembly protein) mRNA, complete cds.	M86667
TTAGCAATAA	350.		
CTGTGCGGAA	351.		
CCTTTGTAAG	352.		
ACACTACGGG	353.	Homo sapiens clone CIR2 cell immortalization-related mRNA sequence.	AF049672
GACGTCTTAA	354.	Human mRNA for proteasome subunit HC9.	D00763
TGAGGCCTCT	355.		
GGAGGGATCA	356.	Homo sapiens integrin-linked kinase (ILK) mRNA, complete cds.	U40282
GGCCCCATTT	357.	Human carbonyl reductase mRNA, complete cds.	J04056 X51
GGCTTTAGGG	358.		
GGGCCAATAA	359.	Homo sapiens full length insert cDNA YN68C05.	AF075046
TGAACCAAGG	360.		
TTTACAGCTG	361.	Human diacylglycerol kinase zeta mRNA, alternatively spliced,	U94905
ACTCTGCTCG	362.		
AGAAAGAAGG	363.		
GAGCAAATGT	364.		
AGAAGTATAG	365.	Human mRNA for proteasome subunit X, complete cds.	D29011
TTTTTAATGT	366.	Human H3.3 histone, class B mRNA, complete cds.	M11354

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
CAGGCTGCCT	367.	Human mRNA for KIAA0249 gene, complete cds.	D87436
CCATTCTCCT	368.		
CCCGGTGTGT	369.		
TTGGTTTTGT	370.		
GAAGTGTGTC	371.		
AGCCTAGGTC	372.		
CTTCTGTCTC	373.		
GCATAGTGTT	374.		
AGAACCAAAA	375.		
AAGAATCTGA	376.	Homo sapiens CI-MNLL homolog gene mRNA, complete cds.	AF054181
CTACAATAAA	377.		
CCGAGTTTTT	378.		
ATTTATTTAT	379.		
TTCCTCCACG	380.	PKC- eta b=protein kinase C eta b [human, monoblastoid U937 cells,	S74620
AGCACTTACA	381.	Human mRNA for lipoprotein apoCII.	X00568
TTCCAAACCT	382.	Human mRNA for phospholipase C.	X14034
GGCCAGTAAC	383.		
GGCTGTACCC	384.	Human cysteine-rich peptide mRNA, complete cds.	M33146
GGCCAGGTGG	385.	Human mRNA for KIAA0047 gene, partial cds.	D38554
GGGAAACCCT	386.	Human replication factor C, 40-kDa subunit (A1) mRNA, complete cds.	M87338
TGGTGGGTGT	387.		
GTGGGCCGCT	388.	Homo sapiens heat shock protein 75 (hsp75) mRNA, partial cds.	AF043254
GTCACTGCCT	389.	Homo sapiens mRNA for Ribosomal protein kinase B (RSK-B).	AJ010119
TACCAGTGTA	390.	Human chaperonin (HSP60) mRNA, complete cds.	M34664
TGGAGGGGCC	391.	Homo sapiens mRNA for CLPP.	Z50853
GCCTTTCTAA	392.	Homo sapiens ribosomal protein S6 kinase 2 (RPS6KA2) mRNA, complete	L07597
GTAGCATAAA	393.		
GGAACACACA	394.		
GAACCGTCCT	395.		
GTCTGGGGGA	396.	Human lysophospholipase homolog (HU-K5) mRNA, complete cds.	U67963
GTCTAGTCAA	397.	Human mRNA for KIAA0179 gene, partial cds.	D80001
CACTCCTACA	398.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TTTGCTCTCC	399.	Human vinculin mRNA, complete cds.	M33308
GTGTACCGGA	400.	Homo sapiens mRNA for Arno protein.	X99753
TAGACAATGC	401.	Homo sapiens clone 23674 mRNA sequence.	AF038183
TTAGATAAGC	402.	Human chaperonin-like protein (HTR3) mRNA, complete cds.	M94083
GTCAACTGCT	403.		
CAGCTCCAAA	404.		
TGGGCCTGGC	405.		
AATGAAAAGG	406.	Homo sapiens testis enhanced gene transcript protein (TEGT) mRNA,	AF033095
TATGTTGCTG	407.		
TCTTCAGGAG	408.		
GTTGTCCATT	409.		
GAAGGTGGGG	410.		
GCGGCGATCG	411.		
CCGAAGGGTC	412.		
GCGAAATCCT	413.		
TGATGCTGAT	414.		
GTTCACATAA	415.		
GATTCAAGTC	416.	Homo sapiens mRNA for mitochondrial ribosomal protein S12.	Y11681
GATCTCATCT	417.		
TGGAGCGATT	418.		
TCCCCCCCCC	419.		
GAGGGCCGGT	420.		
AGAGAAATTT	421.		
GAACCCTGGG	422.		
TGGGTGGGCA	423.		
CGGGTAGTAT	424.	Homo sapiens GAA mRNA for lysosomal alpha-glucosidase (acid maltase).	Y00839
TGTGTGTTTG	425.		
TTGGGTTAAT	426.		
TTGTTTGTAA	427.		
TTTGCAATAA	428.		
TGACCGAACA	429.		
GAGTGAGTGA	430.		
CTTCTCAGGG	431.		
GGGTATCCCT	432.	Homo sapiens RING1 gene.	Z14000
CCCTGAGTTC	433.		
AATATGCTTT	434.	Homo sapiens mRNA for vacuolar H+ ATPase E subunit.	X76228

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
CCGCGTCCCT	435.	Human peroxisome proliferator activated receptor mRNA, complete	L07592
AAATAAAAAG	436.	Homo sapiens full length insert cDNA clone YR51B02.	AF085929
CCACCTGCTT	437.		
CCACACACCG	438.		
ATACATTTAG	439.	Homo sapiens mRNA for Cl1 protein.	X81625
GGGATCAAGG	440.		
AATGCCGCAG	441.		
TCAGTTATCT	442.		
AAGGCAGGGC	443.		
AAACAGTAGT	444.		
CCCCATTCTT	445.		
GGGCGAGAGA	446.		
AATATCTGAC	447.	Human guanine nucleotide regulatory protein (ABR) mRNA, complete	U01147
TGATGTCCAC	448.		
GGGAGTAATA	449.	Human protein tyrosine phosphatase (PTPase-alpha) mRNA.	M34668
TCAGCTGGGG	450.		
CCCCAGCCAG	451.	Human XP1PO ribosomal protein S3 (rpS3) mRNA, complete cds.	U14990
TGGCCCTCCA	452.	Hs.75610: Human transcription factor IL-4 Stat mRN	
TAATAAACAG	453.	Human putative 32kDa heart protein PHP32 mRNA, complete cds.	U47674
TTCATTATAA	454.	Human prothymosin alpha mRNA (ProT-alpha), complete cds.	M26708
GTGTGTTTGT	455.	Human transforming growth factor-beta induced gene product (BIGH3)	M77349
TTTTGGGGGC	456.	Hs.7476: Human mRNA for proton-ATPase-like protein	
TCTCTTTTTC	457.	Homo sapiens tissue specific mRNA.	X67698
CCCACACTAC	458.	Human signal-transducing guanine nucleotide-binding regulatory (G)	M16538 J02
TTCACAAAGG	459.	Homo sapiens mRNA for macropain subunit zeta.	X61970
GTGCCTAGGA	460.		
GGGAAACCCC	461.	Human fibroblast mRNA fragment with Alu sequence (pRHF11).	X05126
CTGACTGTCC	462.	Human major histocompatibility class II antigen gamma chain mRNA,	K01144
GGGGACTGAA	463.	Homo sapiens mRNA for low molecular mass ubiquinone-binding	D50369

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TACTCTTGGC	464.	Human mRNA for novel heterogeneous nuclear RNP protein. L protein.	X16135
GCACTACTCG	465.		
ACTGAAGGCG	466.	Human metargidin precursor mRNA, complete cds.	U41767
CTGGCGCCGA	467.		
GACTATAGCG	468.		
AGGAGCTGCT	469.	Human mitochondrial NADH dehydrogenase-ubiquinone Fe-S protein 8,	U65579
AAGGCCGAGT	470.		
ACGTTTAAGG	471.	Homo sapiens ash mRNA.	X62852
CCTCCAGCAG	472.		
ACTGGTAAAA	473.	Homo sapiens F1Fo-ATPase synthase i subunit mRNA, complete cds.	AF047436
AACTACATAG	474.		
TGCCAGCTAA	475.		
TACGAGGCCG	476.	Homo sapiens mRNA for LAK-4p, complete cds.	AB002405
CTAGCTTTA	477.		
GCTTTCTCAC	478.		
GCTGGCTGGC	479.	Homo sapiens chaperonin containing t-complex polypeptide 1, eta	AF026292
GATCCCAACT	480.	Human mRNA for metallothionein from cadmium-treated cells.	V00594
GGGCCTGTGC	481.	Homo sapiens monocarboxylate transporter (MCT3) mRNA, complete cds.	U81800
TGAGGGAATA	482.	Human triosephosphate isomerase mRNA, complete cds.	M10036 M10
TCTCTCAAAG	483.	Human cell surface antigen (CD53) mRNA, complete cds.	M60871
GGAATGTACG	484.	Human mitochondrial ATP synthase subunit 9, P3 gene copy, mRNA.	U09813
AGAACCTTCA	485.		
TTCTTGTTTT	486.	Homo sapiens mRNA for prion protein, complete cds.	D00015 N00
ACTCCAAAAA	487.	Hs.3655: Human insulinoma rig-analog mRNA encoding	
TCTCAGATGA	488.	Homo sapiens CYP 27 mRNA for vitamin D3 25-hydroxylase.	X59812
TGGCTGGGAA	489.		
TTGTTGTTGA	490.	Human mRNA for calmodulin, complete cds.	D45887

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TGTTCATCAT	491.		
AAAACATTCT	492.		
CTAAAAAAAA	493.	Human 26-kDa cell surface protein TAPA-1 mRNA, complete cds.	M33680
AGATGTGTGG	494.	Human mRNA for mitochondrial 3-ketoacyl-CoA thiolase beta-subunit	D16481
ACGTGGTGAT	495.	Homo sapiens full length insert cDNA clone ZD92G09.	AF086483
CTGCCAACTT	496.	Human cofilin mRNA, partial cds.	U21909
TGCTGCCTGT	497.	Homo sapiens HCG IV mRNA.	X81005
CGTGAGCCAC	498.		
TCTTGTGCAT	499.	Human mRNA for lactate dehydrogenase-A (LDH-A, EC 1.1.1.27).	X02152
AGCAAACTGA	500.		
TGGAAACAAA	501.		
TGTGACCCCT	502.	Human ATP:D-hexose 6-phosphotransferase mRNA, partial cds.	U42303
ATGTTCCTAT	503.		
CTTCTCACCG	504.	Homo sapiens mRNA for ubiquitin-conjugating enzyme UBC9.	AJ002385
AGGTGTGTCA	505.		
CTTCAGAAAT	506.		
GGTCAGTCGG	507.		
TGTAGGTCAT	508.	Homo sapiens full length insert cDNA clone ZD79H11.	AF086432
TACAGAGGGA	509.	Homo sapiens zinc finger protein 216 splice variant 1 (ZNF216)	AF062346
TCAAATGCAT	510.	Human nuclear ribonucleoprotein particle (hnRNP) C protein mRNA.	M16342
CCCAGGGAGA	511.	Homo sapiens chaperonin containing t-complex polypeptide 1, delta	AF026291
GCCAGACACC	512.		
ATCACAGTGT	513.	Human nuclear-encoded mitochondrial serine hydroxymethyltransferase	L11932
ATGGCTAAGC	514.		
GTAGGAGCTG	515.	Human retinal protein (HRG4) mRNA, complete cds.	U40998
AGTCTGATGT	516.		
ATCGCTTTCT	517.	amyloid protein precursor {3' region, alternative polyadenylation,	S41242
GTGGCACGTG	518.	Human clone AZA1 Alu repeat sequence.	U02044
TTGGGGAAAC	519.	Homo sapiens mRNA for biliverdin IX alpha reductase.	X93086
CCTTGGGTTC	520.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
GCAAAGAAAA	521.	Human breast tumor autoantigen mRNA, complete sequence.	U24576
TAAATAATGT	522.	Human Grb2-associated binder-1 mRNA, complete cds.	U43885
GGGAGGATTA	523.	Homo sapiens Tat-interacting protein TIP30 mRNA, complete cds.	AF039103
CACCCCTGAT	524.	Human creatine kinase-B mRNA, complete cds.	M16364
GAGTGGGGGC	525.		
GTAATTACTG	526.		
CGGCCACAGA	527.	Human HepG2 partial cDNA, clone hmd2c12m5.	D16990
AGAATATCAG	528.		
CCATTAACAC	529.		
CAACTTAGTT	530.	Homo sapiens mRNA for myosin regulatory light chain, complete cds.	D50372
ATGCCCGTGA	531.		
AGAGCAAGTA	532.		
GTTGGTCTGT	533.		
TGGAGCAGTT	534.		
TTACCTCCTT	535.		
ATCAAGTTCG	536.		
GAACACCGTC	537.		
CCAAAAAAAA	538.	Human interferon-induced leucine zipper protein (IFP35) mRNA,	U72882
CACAGAGTCC	539.	Human alpha-2-macroglobulin receptor-associated protein mRNA,	M63959
CCTGATGACC	540.		
TATTACTGGG	541.		
TGGCACTTCA	542.	Human low-Mr GTP-binding protein (RAB32) mRNA, partial cds.	U59878
CGACCGTGGC	543.		
CTCTCACCCT	544.	Human mRNA for ribonuclease/angiogenin inhibitor (RAI).	X13973
GGTCCAGTGT	545.	Homo sapiens phosphoglycerate mutase (PGAM-B) mRNA, complete cds.	J04173
GTGGCAGGCA	546.	clone 4-3 {Alu sequences, splice acceptor sites} [human, Pre-mRNA,	S94541
ATTGTTTATG	547.	Human non-histone chromosomal protein HMG-17 mRNA, complete cds.	M12623
GCCTGCTGGG	548.	Homo sapiens GPx-4 mRNA for phospholipid hydroperoxide glutathione	X71973
TTCATACACC	549.	Tag matches mitochondrial DNA	
AAGGAAGATC	550.	Human glutathione-S-transferase	U90313

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
		homolog mRNA, complete cds.	
TGCAGGCCTG	551.	Homo sapiens mRNA for IFN-inducible gamma2 protein.	X59892
TTGTAATCGT	552.	Human mRNA for ornithine decarboxylase antizyme, complete cds.	D87914
CCTCTCCAAC	553.	Human HLA-DMB mRNA, complete cds.	U15085
ATGAGCTGAC	554.	Homo sapiens cystatin B mRNA, complete cds.	L03558
CTGCTAACCC	555.		
AGGTACTGAG	556.		
TGCTGTGTGC	557.	Homo sapiens 15 kDa selenoprotein mRNA, complete cds.	AF051894
TCAGTTTGTC	558.	Human HS1 binding protein HAX-1 mRNA, nuclear gene encoding	U68566
TGCTGAATCA	559.		
GCCCAGCAGG	560.		
CTGTGCATTT	561.	Human 54 kDa protein mRNA, complete cds.	U02493
ATGGTCTACG	562.		
TGAGCCTCGT	563.		
TGGGCCAAAC	564.		
ACATTTTTAA	565.		
AGAGGCAACC	566.		
AGGCAGCGAG	567.	immunoglobulin epsilon chain constant region=membrane-bound form	S55271
CCTGAGGGTA	568.		
GGTTAACGTG	569.		
TTTCAATAGA	570.		
GGTCACACTA	571.		
CGGCCCAACG	572.	Homo sapiens mRNA for arginine methyltransferase, splice variant, 1435	Y10805
TGTGCTAATA	573.	TSE1=protein kinase A regulatory subunit gene [human, mRNA Partial.	S54711
CTGTGCAAGT	574.		
TTATGGGGAG	575.	Human transformation-sensitive protein (IEF SSP 3521) mRNA.	M86752
GTCTTTCTTG	576.		
GAACGCCTAA	577.	Human mRNA for dihydropyrimidinase related protein-2, complete cds.	D78013
GGGGGGTGGA	578.		
GCAGGTCAGC	579.	Human branched chain alpha-keto acid dehydrogenase mRNA, 3' end.	J04474
GATCATCAAG	580.	Homo sapiens mRNA for monocyte	Y10802

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
		chemotactic protein 2.	
TCGTTACGCA	581.		
CGCCTATAAT	582.		
ATCCTCTGCG	583.	Homo sapiens cam kinase I mRNA. complete cds.	L41816
GGCTTTGGAG	584.	Homo sapiens partial mRNA: ID LG141-7B2.	AJ227879
TATTTACTCT	585.		
TATAGGCCGA	586.		
TACACACACG	587.		
TCCTCCCTCC	588.	Human mRNA for proteasome subunit HsC7-I, complete cds.	D26599
TTAATTGGGA	589.	Homo sapiens mRNA for novel glucocorticoid receptor-associated	Z35491
GACCTATCTC	590.		
AGAATCACTT	591.		
AGGAAAAGAT	592.	Human 1.1 kb mRNA upregulated in retinoic acid treated HL-60	U09196
AATGAATGTT	593.		
AATTCTGTAA	594.		
TTTTCTGCTG	595.		
GTGACGTGCA	596.		
GAGGCCACCC	597.		
TACTAATAAA	598.		
ATTAACAAAG	599.	Human mRNA for coupling protein G(s) alpha-subunit (alpha-S1)	X04409
TCCTGCCCCA	600.	Human parathymosin mRNA. complete cds.	M24398
TCTGACAAAC	601.		
TGAATATACT	602.		
TGAGGCAGGG	603.	Human syntaxin 5 mRNA. complete cds.	U26648
TGATGATGTT	604.		
TATATCAGTG	605.		
TATCACTCTG	606.	Human male-enhanced antigen mRNA (Mea), complete cds.	M27937
ACGTCGTGTG	607.		
ACTATTCCAT	608.		
GGTCCCCTAC	609.		
TGGCCTAATA	610.		
TTGAATATTA	611.		
GGGGACACAG	612.		
TTTAGGGGGA	613.		
TTTTACCAGT	614.	Homo sapiens reticulocyte pICln mRNA. complete cds.	AF005422

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TAGCCAGTTA	615.		
TCCGTGTGTC	616.		
GTAAAACCCT	617.		
GTCAGGTTGA	618.	Homo sapiens GOS28/P28 protein mRNA, complete cds.	AF047438
GTTTGAAGGG	619.		
TAGAAGATGC	620.		
GCAAGGGCTA	621.		
GAAGATTGAG	622.	Human signal transducer and activator of transcription Stat5A mRNA,	U43185
TCACAGACTG	623.		
CCTGAAGAGG	624.		
GGGAGCCCGG	625.	Homo sapiens herpesvirus entry protein B (HVEB) mRNA, complete cds.	AF058448
CTTAGAGCCC	626.	Human thioredoxin mRNA, nuclear gene encoding mitochondrial	U78678
TGGTTTGAGC	627.		
CTACCAGGAA	628.		
AACCTGGCCT	629.		
CTGACCTGGG	630.		
TGTGGCCTGC	631.	Human glucose-6-phosphate dehydrogenase (G6PD) mRNA, 3' end.	M35604
TGGCCATCTG	632.		
CAACGTCCTG	633.	Homo sapiens full length insert cDNA YO73E04.	AF075060
AGAAAGTGTC	634.		
ATTCAGCACC	635.		
TGGTGTTGAA	636.		
CAGGGGAGTG	637.	Homo sapiens anpg mRNA.	X56528
CAGTCTGGGA	638.	Homo sapiens mRNA for IL13 receptor alpha-1 chain.	Y09328
ACAAAGTTAC	639.		
AGAGCCCTAG	640.	Homo sapiens COX17 mRNA, complete cds.	L77701
TGTGCCCTGA	641.	Homo sapiens clone 24772 BDP-1 protein mRNA, partial cds.	AF070616
TTGGAGATCT	642.	Human NADH:ubiquinone oxidoreductase MLRQ subunit mRNA. complete	U94586
CTGCTCATCC	643.	Human aldehyde dehydrogenase ALDH7 mRNA, complete cds.	U10868
GATCAATGGA	644.	Homo sapiens oscillin (hLn) mRNA, complete cds.	AF029914
CCTGTCCTTT	645.	Homo sapiens 10kD protein (BC10)	AF053470

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
		mRNA, complete cds.	
CAAAAGGCTC	646.		
CGGAAAAGGA	647.		
GAGCAGTGCT	648.	Homo sapiens RNA for c-fes.	X52192
GCTACCCAAC	649.		
AGCACTGCTG	650.		
AGAGCAAACC	651.	Homo sapiens lysyl hydroxylase (partial clone 2.2 Kb LH) RNA,	M98252
ACTGGAGCCA	652.		
ACAGAAGGGA	653.	Human beta-1D integrin mRNA, cytoplasmic domain, partial cds.	U28252
AAGCTAATAA	654.	Human prostaglandin endoperoxide synthase mRNA, complete cds.	M59979
AAGGAAAGGC	655.	Human manic fringe precursor mRNA, complete cds.	U94352
ACCTTGTGCC	656.	Human L-iditol-2 dehydrogenase mRNA, complete cds.	L29008
CTTGTGTTAT	657.		
GCTATGAGAA	658.	Human binding protein mRNA, 3'end.	L23113
CTGGGTGAAG	659.		
GCGGGAGGGC	660.		
GATCCCAACA	661.	Human mRNA for F1-ATPase beta subunit (F-1 beta).	X03559
TATATATGGG	662.		
GGAGCTTAGA	663.		
AGCTGTCCCC	664.		
AAGATCCAAA	665.		
AAGTAGAAAG	666.	Homo sapiens ATF family member ATF6 (ATF6) mRNA, complete cds.	AF005887
CCTTGACCAA	667.		
GGGGATGGGG	668.		
TTAAAAGTCA	669.		
GGTGGTGGCA	670.		
AACTGTGTTT	671.		
AAAACTGCGT	672.		
AGGGCTTTCA	673.		
GGAGCCAGGC	674.	Homo sapiens GSTT1 mRNA.	X79389
CAACACTGTG	675.		
GGCAGTTAAC	676.		
GGGATGGAGA	677.		
GGAAGGGGGA	678.		
TCTGTTGGAC	679.		
TTGGATATCC	680.		
AAGATAATAA	681.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
GTAAAGCCTA	682.		
GTCAGATGTC	683.		
GTCCATCATA	684.		
GTGGAGCGGA	685.		
GTGGGTCAGC	686.		
TTGAAACCCC	687.		
TAACAGAAAG	688.	Homo sapiens GLI-Krupple related protein (YY1) mRNA, complete cds.	M77698
GGGCCCCAAA	689.		
CGTGTTAATG	690.	Homo sapiens sterol regulatory element-binding protein (CNBP) mRNA,	M28372
GGGATGGCAG	691.	Human G7a mRNA for valyl-tRNA synthetase.	X59303
TGGAACCAGA	692.	Homo sapiens clone 24751 unknown mRNA.	AF070530
CCCTGGGTCC	693.		
CCAATGCACT	694.		
CATTCCAGAG	695.		
CAGCAAAAAA	696.	pyruvate carboxylase [human, kidney, mRNA, 4017 nt].	S72370
CACTTTTGGG	697.	Homo sapiens MLN50 mRNA.	X82456
CACCAGGACA	698.		
CGGAGCCGGC	699.		
GTGTGAGTGT	700.		
TCTTCTGCCA	701.		
TGAGCCCGGC	702.		
TTGTAAAAGG	703.		
TGCCTTAATG	704.	Homo sapiens putative tumor suppressor protein (RDA32) mRNA,	AF061836
TTTACATATA	705.	Homo sapiens mRNA for TIP3, complete cds.	AB000734
TGGGTAAGCC	706.		
TGGTTTTTGG	707.		
TCTCCACGAA	708.	Homo sapiens Arp2/3 protein complex subunit p20-Arc (ARC20) mRNA,	AF006087
TTAAAGATGG	709.		
TATCTATCAA	710.		
TTATATTGCC	711.		
TTCTTCTCGT	712.	Homo sapiens mRNA for SMT3A protein.	X99584
TTCTTCTGAA	713.		
GGAAGAGGGT	714.		
CCTATGTAAG	715.	Homo sapiens mRNA gene for hnRNP G protein.	Z23064

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TGAGGCCAGG	716.	Human high mobility group box (SSRP1) mRNA, complete cds.	M86737
ATCCCCCTGG	717.	Homo sapiens clone 23610 mRNA sequence.	AF052125
ATTGTGAACA	718.	Homo sapiens calcyclin binding protein mRNA, complete cds.	AF057356
TTATAAAAGA	719.		
ATCTTGGTAC	720.		
AGGGGGCAAA	721.	Homo sapiens apolipoprotein L mRNA, complete cds.	AF019225
AATCTGCGCC	722.	Human interferon-induced 17-kDa/15-kDa protein mRNA, complete cds.	M13755
ATACATACTG	723.		
AGGTGCCTCG	724.		
AGGTCCCTGT	725.		
AGGGTGGGGG	726.		
TGTGCTCGGG	727.	Human mRNA for KIAA0088 gene, partial cds.	D42041
GTGGTACAGG	728.	Homo sapiens microtubule-based motor (HsKIFC3) mRNA, complete cds.	AF004426
GCAAAAAAAA	729.	Homo sapiens aortic carboxypeptidase-like protein ACLP mRNA,	AF053944
TACCCCACCT	730.		
CAGTTCTCTG	731.		
AAAAATGGTG	732.		
GTTGGGACAT	733.		
CATTTCATAA	734.	Human mitochondrial ATPase coupling factor 6 subunit (ATP5A) mRNA,	M37104
AATGAAAATA	735.	Homo sapiens breast cancer antiestrogen resistance 3 protein	U92715
ACAGGCAGAA	736.	Human tumor necrosis factor type 2 receptor associated protein	U12597
ACCCTGCCTC	737.		
CATTGAAGGG	738.	Homo sapiens clone 24433 myelodysplasia/myeloid leukemia factor 2	AF070539
ACGAGCTGGA	739.	Human gene similar to Z.mays ras-like (X63277) and Homo sapiens RAY1	AL022729
ACTTCCTCCT	740.		
AGGTGGAGGT	741.		
AGAACCTTTG	742.		
ACATATCTGG	743.		
AGGGTTTGCC	744.	Human mRNA for HLA-A*0218, complete cds.	D83515

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TCTTTCCAGA	745.	Homo sapiens hPTPA mRNA.	X73478
ATGTTTACAC	746.	Human pre-T/NK cell associated protein (5A3) mRNA.	L17329
CCATATACAT	747.		
AGTAGGTGGC	748.		
AGTGAGGATA	749.		
AGTTTTACAA	750.	Homo sapiens 26S proteasome ATPase subunit mRNA, complete cds.	AF038965
ATAGATGGGG	751.		
AGGAAAGCCA	752.	Homo sapiens mRNA for Rab9 effector p40, complete cds.	Z97074
ATCAAGGGGT	753.		
AGCCCAGGAG	754.		
ATGCTAGAAA	755.		
AGGGTGTTTT	756.	Homo sapiens mRNA for MNB protein kinase, complete cds.	D85759
ATTAGCAGAG	757.		
ATTGGAGATG	758.	Homo sapiens mRNA for L-3-phosphoserine phosphatase.	Y10275
CAGAGTGACT	759.	Human IEF SSP 9502 mRNA, complete cds.	L07758
CAGTGGGTGG	760.	Human mRNA for UDP-galactose transporter related isozyme 1,	D87989
AGCTGGTTTC	761.	Homo sapiens Pig8 (PIG8) mRNA, complete cds.	AF010313
CATTGCAGGA	762.		
ATATGTCAGG	763.		
GAGAACCGTA	764.		
GAGGGTTCCA	765.		
GATTGGTATG	766.		
GCCAAGACAC	767.		
CCCGTAATCC	768.		
AGAACTGGAA	769.		
GAATCCAACT	770.		
GCCCGGCTTC	771.		
CCTCTGGCAG	772.		
GCCCAGGGAA	773.		
CCCTCTTTGG	774.		
CCTTTCTGCT	775.		
CGAAAAAAAA	776.		
CGGCTCAAGT	777.	--	
CGGTTCATTG	778.		
CTCCATTGCC	779.		
CTCCTGGAAC	780.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
CTGCTAAGGT	781.		
GTTCTGGGTC	782.		
AGCGTTTCTG	783.		
ATCCGGGGAG	784.	Homo sapiens RCL (Rcl) mRNA, complete cds.	AF040105
CTGACCCGTG	785.		
CTGAGAGATT	786.		
AGGGATGGCC	787.	Human putative T1/ST2 receptor binding protein precursor mRNA.	U41804
GAGGGTATAC	788.	Human mRNA for transcription factor TFE3 (partial).	X51330
GACAGAGAAC	789.		
GAATGAGGAC	790.	Human mRNA for reticulocalbin, complete cds.	D42073
CTGTTAATAA	791.		
CTTTGATCAG	792.		
CTTTTAAAAT	793.	Homo sapiens mRNA for cytochrome c. partial cds.	D00265
GAAACTGAAG	794.	Homo sapiens nitrilase 1 (NIT1) mRNA. complete cds.	AF069987
GAAGTCATTT	795.	Homo sapiens full length insert cDNA clone YZ88A07.	AF086095
CTGCAAGCGG	796.		
AGACAATGTG	797.		
ACTTGATTCA	798.	Human mRNA for KIAA0168 gene, complete cds.	D79990
GCTTAATGTT	799.	Human kidney mRNA for catalase.	X04076
GGGGGTCGGG	800.	Homo sapiens mRNA for protein kinase. PKX1.	X85545
AACTGTATAC	801.	Homo sapiens TAP2E mRNA, complete CDS.	Z22936
AACAATGTCA	802.		
TAAAAGACAA	803.		
GGCTCCTTGA	804.		
GGCCATCTCT	805.		
GGCTGCCCTT	806.		
AAGCGCTCTC	807.		
GCTGGCTGGG	808.		
TAAGGTAGAG	809.		
GGAGGAGCTG	810.		
GCTTTGCAGC	811.	Human Src-like adapter protein mRNA. complete cds.	U44403
GTATTGGCCT	812.		
TATCCTGGCT	813.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
AAAGTGAAGA	814.		
GGGACGGCGC	815.		
GCTACCTTCT	816.		
GCTGCACCGG	817.		
AATCCCCATC	818.		
TAGCAATCAG	819.		
TAGACTTCCT	820.		
TAGACCCCTT	821.	Human endogenous retrovirus type C oncovirus sequence.	M74509
TACTGGAAGT	822.		
TAATAAATGC	823.	Homo sapiens clone 24519 unknown mRNA, partial cds.	AF055000
GTACTGTATG	824.	Homo sapiens importin beta subunit mRNA, complete cds.	L38951
TAACTGCCTA	825.		
AAGAGGAGAT	826.	Human usf mRNA for late upstream transcription factor.	X55666
ACCGGGGTGA	827.		
GGGTAATGTG	828.		
GTTGGACCAG	829.		
ACTCACCTTA	830.		
AAGCTTTGAG	831.		
GTTCACATTG	832.		
GTGGCACGCA	833.	Homo sapiens partial mRNA; ID YG81-2A.	AJ227871
GTGCTGATGA	834.		
TAGGAGAATC	835.	Human vitamin D receptor mRNA, complete cds.	J03258
GTAGCAAAAA	836.		
TGGGGTGGAG	837.	Homo sapiens mRNA for maleylacetoacetate isomerase.	AJ001838
GGGCCCCGCA	838.	Human mRNA for KIAA0123 gene, partial cds.	D50913
TTCTCATAGG	839.		
TGACCTTACC	840.		
TATCCTGGTA	841.	Human isolate 7 clone 10 from Graves' orbital muscle tissue,	U09903
TATTTCGTAC	842.		
TCACTGATGG	843.		
TCCAAGGAAG	844.	Homo sapiens DBI-related protein mRNA, complete cds.	AF069301
TTTGGGGGCC	845.		
TCTGTAAGGG	846.	Human mRNA for KIAA0129 gene, complete cds.	D50919

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TTTCTAAACC	847.		
TCTTTTCAAA	848.		
TGGGCGCCTT	849.	Human uroporphyrinogen decarboxylase mRNA, complete cds.	M14016
TGATCAAAAA	850.		
TGATGCGCGC	851.		
TGCCTGCTCC	852.		
TGCTTGTCAA	853.	Human butyrophilin (BTF5) mRNA, complete cds.	U90552
TGGGAAAGGG	854.		
TCCGCCGCCC	855.		
TTATGTAAAA	856.		
GGAGGACTCC	857.		
TTGATGCCCT	858.		
TGGGTAGCCA	859.		
GGAAGAGCAC	860.	Homo sapiens mRNA for Gal-beta(1-3/1-4)GlcNAc	X74570
TGGTTCCAAA	861.		
AAAGACCAAA	862.		
TGTGTTTGAA	863.		
TTTTCATAAA	864.		
TTACAGTTAA	865.		
TAGCATTTTA	866.	Human mRNA for KIAA0102 gene, complete cds.	D14658
TTGACCGGAG	867.		
GCTTTCTCAA	868.		
TGGGAGAAGT	869.		
TTGCTTGTCC	870.		
TTGTTTAATT	871.	Human capping protein alpha mRNA, partial cds.	U03851
TTTATTGCAC	872.	Homo sapiens mRNA for KIAA0676 protein, partial cds.	AB014576
TTAAGACTTC	873.		
GAACTTTTAG	874.		
CTCACCGCCC	875.	Human cellular retinoic acid-binding protein II (CRABP) mRNA,	M68867
CTAGATTCGG	876.		
CTACAAGAAG	877.		
CGTGGAGTGG	878.		
CGGGCAACGT	879.	Homo sapiens mRNA for rab geranylgeranyl transferase,	Y08200
CGGAGGTGGG	880.	Human mRNA for KIAA0163 gene, complete cds.	D79985

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
CTCATCTGAG	881.	Human E2 ubiquitin conjugating enzyme UbcH5C (UBCH5C) mRNA.	U39318
AAAAAGCTGG	882.		
GAGAGCAGAA	883.		
ATGGCAAAGA	884.		
AAACTGTGGT	885.		
AATGTCATTG	886.		
ACCTGTAATT	887.		
ACGGAACAGG	888.		
ACTGGCCGAA	889.		
ATTACAAAAG	890.		
ACAAGGGTGA	891.		
AAATGTGTAA	892.		
AAAATGCTGA	893.		
ACCCCTGTTA	894.		
AAACTATTTG	895.	Human rab2 mRNA, YPT1-related and member of ras family.	X12953
ACCCCATCGA	896.		
AAAGCAGTTT	897.		
AAAGTGAAAA	898.		
AAAGTTGCTA	899.		
AATACACAGA	900.		
AAATGGCTAA	901.		
AACTACCAAA	902.		
ACTGTTTGTT	903.	Human mRNA for HLA-D class II antigen DPW2 beta chain.	X03067
GAGAAGTTAC	904.		
AAACCTCAGG	905.		
ACTGTGGTCA	906.		
CTCAGCAGGA	907.		
CGAGTTTTTT	908.		
CTCCTGCCTT	909.		
CTCGGCCAGA	910.	Human mRNA fragment for apolipoprotein E (apo E).	X00199
CTCGTCCGGA	911.		
CTCTCAGGGG	912.		
CTGCCTCCGT	913.		
CTGCTGCACT	914.		
ACCCTCTGTG	915.		
ACCAAGAGCA	916.		
CTGTTTCAGA	917.		
AATACACATC	918.		
AATATGGGTG	919.	Human tetratricopeptide repeat protein (tpr2) mRNA. complete cds.	U46571

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
AATATGGTTT	920.		
AATCTTGCAA	921.		
AATGCTGGCA	922.	Homo sapiens mRNA for MSJ-1, complete cds.	AB014888
AAGGGCCGGT	923.	Homo sapiens mRNA for immunoglobulin heavy chain. VHDJH	AJ008244
ACATTTCAAT	924.		
AAGGATGCGG	925.		
CTCAGCAAAA	926.		
CAGTTACAAA	927.		
ATTGGTTATG	928.		
ATTGATCAAT	929.		
ATTCTGCCCA	930.		
GATAGGATAA	931.		
CACAAACCGG	932.		
CCACTGCAAT	933.		
CCTTTGTAAA	934.		
CCTTTAATCC	935.	Homo sapiens (xs88) mRNA, 318bp.	Z36845
CCTCTCTCCT	936.	Homo sapiens Staf50 mRNA.	X82200
CCGCCTTAAT	937.		
CCGAACACGG	938.		
CCAGAAAGAA	939.	Homo sapiens TIMP3 mRNA for tissue inhibitor of metalloproteinases-3.	X76227
CCCAGCCTCA	940.		
CAAATCCAAA	941.		
CAGTTAGTAA	942.		
CCACTCTGGC	943.	Homo sapiens mRNA for processing a-glucosidase I.	X87237
CCACGCACCA	944.		
CCAAGGACTC	945.	Human SUPT4H mRNA, complete cds.	U38817
CATTTTTCCC	946.		
CATTCATTGG	947.		
CATCAGGATA	948.		
ATGTACTAAA	949.	Homo sapiens mRNA for TFG protein.	Y07968
CCCACTGCCC	950.		
AACTCTGTAA	951.		
TGGCCAAAAA	952.		
CCCTATAAGC	953.		
CGAGAGCTGC	954.		
GACCCTGGGG	955.		
GACATAAATC	956.	Human mRNA for KIAA0113 gene, partial cds.	D30755
GACACCTCCT	957.		
CTGGAAGCTC	958.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
GAATCACTGC	959.	Homo sapiens ribosomal protein L35-like protein mRNA, complete cds.	AF047440
CTGGGGGTCT	960.		
GAACCCTTCT	961.		
GAACAAAAAA	962.		
CTTTTTGGAA	963.		
CTTTTCTTTA	964.	Human GTF3A mRNA for Xenopus transcription factor IIIA homologue.	D32257
CTTGTAGTCC	965.		
ATTTCTTGCC	966.		
CTTCATAAGT	967.		
ATTTGCCTCT	968.		
GAATGTAAGT	969.		
CAATTAATAC	970.		
CAGCGGAAGC	971.		
CAGCCTTGCG	972.		
CAGATGCAAA	973.		
CAGATACCCC	974.		
CACGATTAAA	975.		
CACCGGGTAG	976.	Homo sapiens nonsense-mediated mRNA decay trans-acting factor mRNA,	AF074016
CGGACAATCA	977.		
CACAAACACA	978.		
CATACACTCT	979.	Homo sapiens Humig mRNA.	X72755 S60
GACTAGTGCG	980.		
GATTTTCTGG	981.		
GCCGGCTCTT	982.		
GCAAAACTCT	983.		
TGTTAATGTT	984.		
GCTGGCAGAG	985.		
GGCTGAGAAT	986.		
GCGAACTCCG	987.		
GCGCGGCTAC	988.		
GCGCTGCTTT	989.		
GCGGTAAAAA	990.		
GCTAGTGAAA	991.		
GCTCAGGATG	992.		
TTATGGGGAT	993.		
GCTGCAGGGG	994.		
TTACTCTTTC	995.	Homo sapiens mRNA for aldehyde dehydrogenase (using	X75425
GCTTGTAAAA	996.		
GCTTGTAGCC	997.		
GGAATAAATT	998.	Human mRNA for cytochrome c1.	X06994

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
GGAATCCTGT	999.		
GGAGAGGGCA	1000.		
GGAGTAGGAA	1001.		
TAAACTGAAA	1002.		
GCTCTCCCCT	1003.		
GCACTCTATG	1004.	Human interleukin-8 receptor type B (IL8RB) mRNA, complete cds.	M73969
GATATCAAAA	1005.		
TTGGGGTATC	1006.		
GCCTCTTCCC	1007.		
TGGGCTACTC	1008.		
TGGACCAGTG	1009.		
TTGGTCATCC	1010.		
TTCAGCAGAG	1011.		
TTGGTGATAC	1012.		
TTGTAAATAG	1013.	Homo sapiens Golgi complex autoantigen golgin-97 mRNA, complete	U51587
TTTACAGGGT	1014.		
TTTATTCCCT	1015.		
AAGATAATGC	1016.		
TTTTTCTGGC	1017.		
TCTGAAGTGG	1018.		
GTTTGCAAGT	1019.		
TGGCGTTGAG	1020.		
GCAAAACTTT	1021.		
TGTAGGAAAC	1022.		
TGTATGGTGG	1023.		
TGTATTACAG	1024.	Homo sapiens mRNA for novel DNA binding protein.	X63071 S50
TGTCTCCTTC	1025.		
TGTGAGCAGA	1026.		
TTCAGTGCCT	1027.		
TGTTCCTGAG	1028.		
TTCAGCGTTC	1029.		
TTAAAGTCAA	1030.		
TTAACAATTC	1031.		
TTACACTGGA	1032.		
TGTTTTTATG	1033.		
GGTTCAGTTA	1034.		
GATCCGCTCT	1035.		
GTTGGTCCCT	1036.		
GTTGTTAACA	1037.	Homo sapiens heparan sulfate 3-O-sulfotransferase-1 precursor	AF019386
AGGAGGGATA	1038.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
GTGTCAGATA	1039.		
GTATATAACT	1040.		
GGGAAGGGGG	1041.		
GGGAAGTCAC	1042.	Human FX protein mRNA, complete cds.	U58766
GGGCGGGGGC	1043.	Human DNA polymerase delta catalytic subunit mRNA, complete cds.	M80397
GGGGACTCCG	1044.		
GTTGAGTAAC	1045.		
GGTACAAATA	1046.		
GTTATTGAGG	1047.		
GTGACTCGCA	1048.		
GTACTTACCT	1049.		
GTGACCTTCT	1050.		
GTATCTTAAT	1051.		
GTATGGAAGA	1052.		
GTATGTAACT	1053.	Human mRNA for high affinity Fc receptor (FcRI).	X14356 M21
GTCTGCCTGG	1054.	Homo sapiens metase (MET-1) mRNA. complete cds.	L23134
GTGAAAAACA	1055.		
GTTTTCATTC	1056.		
GTACATTGTA	1057.		
AGGCCTGCCA	1058.		
GGGGGCAGTG	1059.		
GCACACTAGC	1060.		
GCAACAACAC	1061.		
GCAACTGTGA	1062.		
GCAAGAATTT	1063.		
GCCTGAGGGG	1064.		
GCACCTATTG	1065.		
GGGAAGATCT	1066.	Homo sapiens mRNA for ERp28 protein.	X94910
GCAGTGCCAA	1067.		
GCATTCGCAG	1068.		
GCATTTTGTG	1069.		
GCCAATTGGG	1070.		
GTTGGGTAGA	1071.		
GCCCTGGAAA	1072.		
TTTTGTTAAT	1073.		
GTTATAATAC	1074.	Homo sapiens mRNA for putative serine/threonine protein kinase.	Y10032
GTGATCATTA	1075.		
GTGCCCCTTC	1076.		
GTGCTCATTC	1077.	Homo sapiens mRNA for TGF-beta superfamily protein, complete cds.	AB000584

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
GTGGCAGATG	1078.		
GTGGGTGTCC	1079.		
GTGGTGCGCG	1080.		
GTGGTGTAGG	1081.		
GGCCACCCTG	1082.		
GTTAAAACAG	1083.		
GTGACAGAAT	1084.	Human uridine diphosphoglucose pyrophosphorylase mRNA, complete	U27460
GCCCCTTGCA	1085.		
AGCTGCCGCA	1086.		
TGAATTCTAC	1087.		
AGAAATACCA	1088.		
AGAGCTCACT	1089.		
AGCAAGCCCC	1090.		
AGCACAGAGG	1091.	Homo sapiens citrate synthase mRNA, complete cds.	AF047042
AGCACATTCT	1092.		
TTGGTAAAGA	1093.		
AGGGCAGAGG	1094.		
TTGGGCAATA	1095.		
AGCCTTTGTT	1096.	Human mRNA for collagen binding protein 2, complete cds.	D83174
AGCTAAGTTT	1097.		
ATATGTTGAC	1098.		
AGCTGCTGGT	1099.		
AGGACAGAAG	1100.		
AGGATGGCGG	1101.		
GATAGGTCGG	1102.	Homo sapiens mRNA for iron regulatory factor.	Z11559
AGCCCTAGTA	1103.		
TGATGTGATA	1104.		
TGGAGTGAAG	1105.		
TCTTGCCTAG	1106.		
TCTTTTGAAT	1107.		
AGGGAGACCT	1108.		
ATATGAAGCA	1109.		
AAGCGAGACG	1110.		
AAGGAAGATT	1111.		
AAGGACTCCG	1112.		
AAATCAATAA	1113.		
ATCATTGTGG	1114.		
AGTCTCTCTT	1115.		
AGTGCAAACG	1116.		
AGTTTCTTGA	1117.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
ATACAATAAA	1118.	Human gene for PP15 (placental protein 15).	X07315
ACTTACATTA	1119.		
ATAGCCTCTT	1120.		
AGCCTGTTGC	1121.		
ACTGGGCGCC	1122.	Human mRNA for KIAA0358 gene, complete cds.	AB002356
ATCAGCTGCT	1123.		
AGGCTAGACC	1124.		
ATCCGCCTGC	1125.		
ATCGATCGCC	1126.		
ATCGTTGTAA	1127.	Homo sapiens mRNA for ATP-dependent RNA helicase #46, complete cds.	AB001636
ATGAATATTC	1128.	Homo sapiens partial mRNA; single read (clone A3351).	Z50170
ATGAGCTATG	1129.		
ATGCGCAAGG	1130.	Homo sapiens (xs13) mRNA, 284bp.	Z36785
ATACAGGTCT	1131.	Homo sapiens mRNA for DNA binding regulatory factor.	X85786
AGCACCAGAA	1132.	Homo sapiens mRNA for KIAA0690 protein, partial cds.	AB014590
TATTTATATG	1133.	Homo sapiens cig41 mRNA, partial sequence.	AF026943
TACATACGTC	1134.		
TACTCCAAGC	1135.		
TAGATGTGAT	1136.		
TAGCTGAGAC	1137.	Human Rch1 (RCH1) mRNA, complete cds.	U09559
TAGGTCCTCT	1138.		
TATAAATAAA	1139.	Human mRNA for KIAA0130 gene, complete cds.	D50920
TATGGGTTCC	1140.	Homo sapiens full length insert cDNA clone ZC19E11.	AF088028
TATTTTACGT	1141.	Homo sapiens RNA polymerase II elongation factor SIII, p15 subunit	L34587
TGATCACTGC	1142.		
TGACATTCCC	1143.		
TAAATACAGT	1144.		
TCAGTGAACG	1145.	Human mRNA for motor protein, partial cds.	D21092
TCAGTTCTGA	1146.		
TCCACCAGTT	1147.		
TCCGAAACCT	1148.		
TATATTGAGA	1149.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TTGGTGAAGA	1150.		
TTCCCTCGTG	1151.		
TTGAACACTT	1152.		
TTGAATCGTG	1153.		
TCAGCAGGGC	1154.		
TTGCCTGGAT	1155.		
TGCGTTGAGA	1156.		
TGACCTGTGT	1157.		
TGCCTTACAG	1158.		
TGATGTTTGC	1159.		
TGCCGTGCCT	1160.		
TGCCCTGAGA	1161.	Homo sapiens cytochrome oxidase assembly factor (PET112) mRNA,	AF026851
TGCATATCAT	1162.	Homo sapiens mRNA for CRM1 protein, complete cds.	D89729
TGATGGGCAT	1163.		
TCCTTCTGTG	1164.		
TCCTCCCTAC	1165.		
TTGGAAACCT	1166.		
TGAGGAGCTC	1167.		
GAGGCCGGCC	1168.		
AAGCACAAAA	1169.	Homo sapiens DNAX activation protein 12 (DAP12) mRNA, complete cds.	AF019562
GGGGCAGGGC	1170.		
CCCAGCTAAT	1171.	Human 15-lipoxygenase mRNA, complete cds.	M23892
GCTCCCAGAC	1172.	Homo sapiens mRNA for synaptogyrin 2.	AJ002308
AGGCGAGATC	1173.		
CCATTGCACT	1174.	Homo sapiens full length insert cDNA YQ02E12.	AF075065
TGCGAGGAGA	1175.	Homo sapiens mRNA for renin-binding protein, complete cds.	D10232 D01
GTACGTCCCA	1176.	Human neutral amino acid transporter B mRNA, complete cds.	U53347
AATCAACTTG	1177.		
TGCGCGCCCT	1178.	-	
CAGGATGACG	1179.		
GGCGGGGACA	1180.		
CCACTCCTCA	1181.	Human mRNA for DAD-1, complete cds.	D15057
AGAGGTTGAT	1182.		
GGTGAGACCT	1183.	neuropolypeptide h3 [human, brain, mRNA Partial, 723 nt].	S76773
CAGGAACGGG	1184.	Homosapiens ERK activator kinase (MEK2) mRNA.	L11285

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
CCAATTTGCA	1185.		
GTTTCTTCCC	1186.		
GGATGTGAAA	1187.	Human mRNA for T-cell surface glycoprotein E2.	X16996
GTGGCGCACA	1188.	26 S protease subunit 5b=50 kda subunit [human, HeLa cells, mRNA	S79862
GATTAATGTG	1189.	Homo sapiens ICB-1 mRNA, complete cds.	AF044896
GAATTTCCCA	1190.	Human mRNA for complement component C2.	X04481 K01
TGTGAACACA	1191.	Human mRNA for interferon regulatory factor 1.	X14454
CGGCTGAATT	1192.		
GGAAGATGTT	1193.		
GGAAGCACGG	1194.	Human antisecretory factor-1 mRNA, complete cds.	U24704
GGAAGGGGAG	1195.	Homo sapiens mRNA for NF-kB subunit.	X61498
CTAACCAGAC	1196.	Human F-actin capping protein beta subunit mRNA, complete cds.	U03271
TACCCCTCTC	1197.	Homo sapiens phospholipase C-beta-2 mRNA, complete cds.	M95678
TGGAGGCCAG	1198.		
GTGACAGACA	1199.	Human nuclear factor NF45 mRNA, complete cds.	U10323
TCACGGCAAG	1200.		
ATTGTGCCAC	1201.		
AGACAGAGTG	1202.		
ACCTGCTGGT	1203.	Homo sapiens clone 23675 mRNA sequence.	AF052113
CCTTACTTTA	1204.		
TGAACCCGCC	1205.		
ACCTCAGGAA	1206.	Human high density lipoprotein binding protein (HBP) mRNA, complete	M64098 M83
GACCCTGCCC	1207.	Human FK-506 binding protein homologue (FKBP38) mRNA, complete cds.	L37033
TGTGATCAGA	1208.	Homo sapiens F1F0-type ATP synthase subunit g mRNA, complete cds.	AF092124
TCCTTCTCCA	1209.	Human mRNA for alpha-actinin.	X15804
AGCCTGCAGA	1210.		
GCTGCCCTTG	1211.	human alpha-tubulin mRNA, 3' end.	K00557
ACAAACTTAG	1212.		
CTCGGTGATG	1213.	Homo sapiens mRNA for ras-related GTP-binding protein, complete	D78132

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TTCTGGCTGC	1214.	Human mRNA for core f protein, complete cds.	D26485
CCAGGAGGAA	1215.	Hs.103424: HEAT SHOCK COGNATE 71 KD PROTEIN	
GTGAAGCCTC	1216.		
CTGAGACACC	1217.		
GGGAGGGGTG	1218.		
TGGAGAATGT	1219.		
TGTGCACCCC	1220.	Homo sapiens clone 24574 mRNA sequence.	AF052151
TTGATTTCTT	1221.	Human MHC class II HLA-DQA1 mRNA, complete cds.	M33906
GTCATTTGGA	1222.		
TGGTCTGGAG	1223.	Human mRNA for KIAA0216 gene, complete cds.	D86970
ATGGCACACA	1224.	Homo sapiens class I cytokine receptor (WSX1) mRNA, complete cds.	AF053004
AGATGAGAAA	1225.		
TCTGCAAATT	1226.		
GCAACATCAG	1227.		
CATCTCTAGT	1228.		
GCAGCCCCAA	1229.		
GGAATACGCA	1230.		
TAGAAGGTGG	1231.		
TCAAAGCCAT	1232.		
AGGGCTTCAA	1233.		
CGCCTCCGGG	1234.		
GGTAGCAGGG	1235.		
CCCATTTGCA	1236.		
AATGCTTTGT	1237.		
CCTGCACCCA	1238.	Human Sel-1 like mRNA, complete cds.	U11037
TTCCAGACCT	1239.	Human HepG2 3' region MboI cDNA, clone hmd1d12m3.	D17127
TTGTACAACA	1240.		
TTTCCACCCG	1241.		
GTGGCGGGCG	1242.	Homo sapiens mRNA for KIAA0565 protein, complete cds.	AB011137
ACAGCTAACA	1243.		
ACCGCCTGTG	1244.		
ATGGTTTTTG	1245.		
ACGGTGATGT	1246.		
TCTTTGTAGG	1247.		
CCTTTTTAGT	1248.		
ACTACCACCC	1249.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TTCAAAAAGG	1250.		
TGTCAGAGAT	1251.		
TGATGTGATC	1252.	Homo sapiens GT197 partial ORF mRNA, 3' end of cds.	L38932
TGAAGAGAAG	1253.	Human mRNA for KIAA0106 gene, complete cds.	D14662
TGAAAGTGTG	1254.	Homo sapiens antigen NY-CO-25 (NY-CO-25) mRNA, partial cds.	AF039695
CAATACATAC	1255.		
TATGACTTAA	1256.	Homo sapiens calcium-activated potassium channel (KCNN3) mRNA.	AF031815
GTGAATGACG	1257.		
GTCCCAACAC	1258.	Homo sapiens full length insert cDNA clone ZD73F11.	AF086389
GGCCCTGCAG	1259.		
GCTTACCTTT	1260.		
GCCTGGGCTG	1261.		
GAGCTCTGAG	1262.	Homo sapiens dysferlin mRNA, complete cds.	AF075575
GCCTCCACAG	1263.		
TTACAATTTG	1264.		
GGCTCCTCGA	1265.	Homo sapiens tapasin (NGS-17) mRNA, complete cds.	AF029750
TCGATGTGGG	1266.		
TGTGCCCTGT	1267.		
GACACCAACT	1268.	Homo sapiens deubiquitinating enzyme UnpEL (UNP) mRNA, complete	AF017305
ACACTTACAA	1269.	Homo sapiens UEV1Bs (UBE2V) mRNA, alternatively spliced, partial	U97280
GGAGAAGATG	1270.		
GACAGTCCTG	1271.		
GAGAGCTACA	1272.	Human electron transfer flavoprotein alpha-subunit mRNA, complete	J04058
GGGTCTGTGA	1273.		
TATGCTGTTA	1274.		
GTTGTGGTTC	1275.		
TCATAACTGT	1276.	Human mRNA for flavoprotein subunit of complex II, complete cds.	D30648
GAGCCAACCC	1277.		
TGAGTGACAC	1278.		
ACCTGTGACC	1279.	Homo sapiens mRNA for pro-urokinase precursor, complete cds.	D00244
TGCCTTAGTA	1280.		
TGGAGGTGGG	1281.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
GCGGACGAGG	1282.	Homo sapiens TFAR19 mRNA, complete cds.	AF014955
TGGGGATTAC	1283.		
TCAATCAAGA	1284.	Human 14-3-3n protein mRNA, complete cds.	L20422
GCGGACTGGG	1285.		
GCCTCTGCCA	1286.	Human mRNA for KIAA0272 gene, partial cds.	D87462
GCCGAGTCCA	1287.	Homo sapiens leukocyte-associated Ig-like receptor-1 (LAIR-1) mRNA,	AF013249
GCCCTTGCAA	1288.		
GCCCTGGGTG	1289.		
GGCCGTGTGA	1290.		
TGCAGTGACT	1291.	Homo sapiens mRNA for 37 kDa LIM domain protein.	X93510
ACAGTGCTTG	1292.	Human mRNA for protein phosphatase 2A (beta-type).	X12656
AAGTCGCTCA	1293.		
TAGTTGTAGG	1294.		
TAATAAAGAA	1295.	Human mRNA for cytokeratin 15.	X07696
TGGGTGTTGA	1296.		
GGAAGGGAGG	1297.		
GATGTTGTCC	1298.		
GGCCAGGAAG	1299.		
GGGAGCCGAG	1300.	Human mRNA for KIAA0169 gene, partial cds.	D79991
GGGGGCTGCT	1301.		
GTGCACTGAA	1302.		
GTGGACCCCA	1303.	Human siah binding protein 1 (SiahBP1) mRNA, partial cds.	U51586
GTGTCTCATC	1304.	Homo sapiens mRNA for 2-phosphopyruvate-hydratase-alpha-enolase.	X84907
GTTTAAAAGA	1305.		
ATGGTTAAAG	1306.		
CTGGAGAACA	1307.		
TGGCAGGTTC	1308.		
CTAAATATAG	1309.		
CGCTTTTGTA	1310.		
CGAATTGAGA	1311.		
CCTGTCCTGC	1312.		
CCTCTTTAAA	1313.	Human mRNA for KIAA0140 gene, complete cds.	D50930
CCCATCGTCT	1314.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
ACAGCCACTG	1315.		
TGTGTCAAAG	1316.		
GAAGATTAAT	1317.	Homo sapiens sorting nexin 3 (SNX3) mRNA, complete cds.	AF034546
CTGGGTTGTG	1318.		
ATGGAAAGGA	1319.		
ATCCACCCAC	1320.	Human telomeric repeat DNA-binding protein (PIN2) mRNA, complete	U74382
AGGGAGAGGG	1321.	Homo sapiens mRNA for de-ubiquitinase.	X91349
AGGCTGCGAC	1322.		
AGGATTAAAA	1323.		
AGGATGTGGG	1324.	Human kinesin-like motor protein KIF1C mRNA, complete cds.	U91329
AGCAGCCGCT	1325.		
AGACCAAAGT	1326.	Human mRNA for heat-shock protein 40, complete cds.	D49547 D17
AGAAGCCAGA	1327.		
CACTGTGTTG	1328.		
TTACCCAGGC	1329.	Human UMP synthase mRNA, complete cds.	J03626
CAGCGCACAG	1330.		
TTGACCTGTG	1331.		
TTTGTGCACT	1332.		
TCGGGAGCTG	1333.		
ATGTTGTACT	1334.		
CTGTTGCATT	1335.		
CTCTGCTCGG	1336.		
TTTCAGGGGA	1337.		
TTCTCTCAAC	1338.		
TATTTTAAAT	1339.		
GTCTACCTGA	1340.		
GGCATTGGGG	1341.		
TTCTCTTTCA	1342.		
TGTCTAACTA	1343.		
TGGTGGAATG	1344.		
GTCCCCCCAA	1345.		
GTATCTTCAG	1346.		
GTATAATTTG	1347.		
TAACAAAGGA	1348.		
TGTGAATTTT	1349.		
TGTGCGCGGG	1350.		
TGTTAGCCTG	1351.		
TTACAACATT	1352.		
TTTGTGACTG	1353.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
GGCGCCTTCT	1354.		
GGGGCTGGAG	1355.		
GGAGATGAAG	1356.	Human SLP-76 associated protein mRNA, complete cds.	U93049
GGAGATGCCT	1357.	Human interleukin 3 receptor (hIL-3Ra) mRNA, complete cds.	M74782
GTGGAGGTGC	1358.	Human 100 kDa coactivator mRNA, complete cds.	U22055
GGCAAAGAGG	1359.		
GGCACAGTAA	1360.	Homo sapiens full length insert cDNA clone ZD76B08.	AF086406
GCTTTCATTG	1361.		
GGTTACATTA	1362.		
TTCACTGTAG	1363.		
GTCTGCCTCA	1364.		
GGAATGAGAA	1365.		
GGGTTTGAAC	1366.		
GGAGAGTACA	1367.		
GGTTATCTGT	1368.		
GTAGATGCAA	1369.	Human transcription factor (ITF-1) mRNA, 3' end.	X52078 M30
GGCAGAAGAT	1370.		
GGGGGTCACC	1371.	Human mRNA for ATP synthase subunit c encoded by P1 gene.	D13118
GTGCGTGCCT	1372.		
TAGGTTGTCA	1373.		
GTTGCGGTTA	1374.		
GTTGGAGGCC	1375.		
GTTTCTCTGG	1376.		
GTTTTGTACA	1377.		
GCTGGGACAG	1378.		
GTGATGCTGG	1379.		
GTGGACTTTT	1380.		
TACCCGCCTC	1381.		
TACTAAAAAA	1382.	Homo sapiens NADH-ubiquinone oxidoreductase NDUFS2 subunit mRNA,	AF050640
GTTTGACAGA	1383.		
GCTGGCAGGC	1384.		
TGGGGGGTTT	1385.		
GGACCCTCTC	1386.	Homo sapiens clone 23764 mRNA sequence.	AF007133
TAACCTGCTA	1387.		
ATAGCTGGGG	1388.	Homosapiens ERK activator kinase (MEK1) mRNA.	L11284

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TTGATGGTGC	1389.		
CAATGGAGCT	1390.		
CAAGCTGTAA	1391.	Human HepG2 3' region Mbol cDNA. clone hmd5a09m3.	D17249
ATTGTCAGGG	1392.		
ATTGGCTGGG	1393.	protein phosphatase 2C alpha [human. teratocarcinoma. mRNA. 2346	S87759
CAGGACGGGC	1394.	Homo sapiens encoding CLA-1 mRNA.	Z22555
ATGGGAACCA	1395.	Homo sapiens mRNA for GTP-binding protein.	X80754
CAGGAGACAG	1396.		
ATATTGATGA	1397.		
ATATATTCAG	1398.		
ATATAGTCAG	1399.	Human mRNA for KIAK0002 gene. complete cds.	D13639
ATAAATAAGG	1400.		
AGGTTTTCAT	1401.		
AGGGGCGCAG	1402.	Homo sapiens mRNA for protein containing SH3 domain, SH3GL1.	X99656
AGAGCCAAGT	1403.		
AAAGAGAAGA	1404.		
AAGGGTGCCA	1405.		
TGTTCCCTTT	1406.	Human MXI1 mRNA, complete cds.	L07648
AGCTGATCAG	1407.	Human mRNA for acylamino acid-releasing enzyme, complete cds.	D38441
AAGGAAAGTG	1408.	Homo sapiens DEC-205 mRNA, complete cds.	AF011333
AACGCTGCCT	1409.		
CACACCAATT	1410.		
AAAGGTTGGT	1411.	Human mRNA for KNP-Ia, complete cds.	D86061
ATTGACCGCT	1412.		
AAAAGATACT	1413.		
CCTTTCTCTC	1414.	Human mRNA for KIAA0068 gene, partial cds.	D38549
TTTTGTACCA	1415.		
AATGCTGTGA	1416.		
ATGGCGATCT	1417.		
CAGTCTCAGA	1418.		
AACAGAATAT	1419.	Homo sapiens GA17 protein mRNA. complete cds.	AF064603
TTTTATCTGG	1420.	Homo sapiens mRNA for ITBA2 protein.	X92896
TCCTTCTACG	1421.		
TCCATCGTCC	1422.		
TCATACTGAA	1423.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TCAGCAAGGG	1424.		
TCAAGTCACC	1425.		
AGGGCCCTCA	1426.		
TTCTCCCCCT	1427.	Human mRNA for KIAA0339 gene, complete cds.	AB002337
TCTGTAGCTA	1428.		
TTTTAAACTT	1429.		
AGTTGAAATT	1430.		
GTGTAAATGG	1431.		
TACTGGCTCA	1432.		
GTGGCGGGAG	1433.	Homo sapiens mRNA for RAP74.	X64002
GTTATTCCCC	1434.		
TGACTGGCAG	1435.	Homo sapiens mRNA for IL-1/TNF inducible EST (clone MEC-205).	X84805
TGCCCAGACC	1436.		
AGCCACCTCA	1437.		
TGAACCGTT	1438.		
TGGGATGACA	1439.		
TGGGAACCTA	1440.		
TGGCTGTGAG	1441.	Human chromosome 17q12-21 mRNA. clone pOV-3, partial cds.	U18920
TGGCCTAAAA	1442.		
TCTCTGCAAA	1443.		
TGCTTGGCTT	1444.	Human mRNA for small GTP-binding protein, S10, complete cds.	D14889
TCTGCATAGA	1445.		
TGATCTGCCT	1446.		
TGAGGAGCTG	1447.		
TCAAACTGTG	1448.		
TGACTGAAGC	1449.	Homo sapiens 3-phosphoglycerate dehydrogenase mRNA, complete cds.	AF006043
TGTAGTATTT	1450.		
AGGCTTTAGG	1451.		
TGGCAAAATG	1452.		
CTACCAGCAC	1453.		
AATTGTGCAT	1454.		
GATGAGAAGA	1455.		
GCGGGAGCGG	1456.	Human mRNA for KIAA0224 gene, complete cds.	D86977
CCGCCCTCTA	1457.		
CCGGCCAGCG	1458.		
CCTATGGCTT	1459.		
CCTGGCAGTT	1460.		
CGAAGTGTCC	1461.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
CGCGCACCCG	1462.		
CGCGTCACTA	1463.		
GAAGCTGCCT	1464.	Homo sapiens leucocyte immunoglobulin-like receptor-5 (LIR-5) mRNA.	AF025532
CGGTTTGCAG	1465.		
GCCTGTGCTG	1466.	Homo sapiens Huntington's Disease (HD) mRNA, complete cds.	L12392
CGTTTTCTGA	1467.	Homo sapiens protein tyrosine phosphatase (PRL-1) mRNA, 3' end of	L39000
GCGCGGGCGA	1468.		
CTCGGCGAGC	1469.		
CTGCAGAGTG	1470.	Human putative holocytochrome c-type synthetase mRNA, complete cds.	U36787
CTGCGTGATG	1471.		
CTGGATCTGG	1472.	Human fetal brain glycogen phosphorylase B mRNA, complete cds.	U47025
CTGGTCCTCC	1473.		
CTTAAGACTT	1474.		
CTTTCAAAAC	1475.		
CGGTGTTGAG	1476.		
CCTCCCCGAA	1477.		
TTTGTTGTAT	1478.		
TTTCTCTCCT	1479.	Human transcription factor NFATx mRNA, complete cds.	U14510
TTGTGATGTA	1480.		
TTGGTGAGGG	1481.		
CCCCTCTGAG	1482.	Homo sapiens IFI-4 mRNA for type I protein.	X79448
AGAAGTGTCT	1483.		
GCCTCCAGGG	1484.		
GAGCACATCC	1485.		
CGTCTCCACA	1486.		
GAGAGCTGGG	1487.	Homo sapiens P2Y6 receptor, short splice variant mRNA, complete	AF007891
CCAGATGTGT	1488.		
GATTTCTATT	1489.		
GAGCTTACCC	1490.		
CCCTTCCCCG	1491.		
GAGCACTGTT	1492.		
ACTTGATTTG	1493.	Homo sapiens mRNA for KIAA0494 protein, complete cds.	AB007963
ACGTGTCTAT	1494.	Human clone 23612 mRNA sequence.	U90902
ACCCTCCTCT	1495.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
ACCAGAACAG	1496.		
ACCACAAATG	1497.		
ACACACCTGG	1498.		
AAGGCACAGA	1499.	Homo sapiens phosphatidylinositol synthase (PIS) mRNA, complete	AF014807
GCAAAATAAC	1500.	Human initiation factor 4D 9eIF 4D) mRNA, complete cds.	M23419
GCCCTGATTT	1501.	Human interferon regulatory factor 5 (Humirf5) mRNA, complete cds.	U51127
GCCCCACAGC	1502.		
GCCAAGATGC	1503.		
GAGATCCACG	1504.	Human zinc finger protein mRNA, complete cds.	L16896
GCATATTAAA	1505.	Human mRNA for XP-C repair complementing protein (p58/HHR23B).	D21090
GAGGAGCCCC	1506.		
CTTTTAAGAA	1507.		
GATGAGTGGA	1508.	Human adrenodoxin mRNA, complete cds.	J03548
GAAACTGGAA	1509.		
GAGGTGGGGC	1510.		
GCCAAAAAAA	1511.	Homo sapiens (TL7) mRNA from LNCaP cell line.	X75687
TGTGTTGTCA	1512.	Human mRNA for NAD-dependent methylene tetrahydrofolate	X16396
GTGATGGTGT	1513.	Human lupus p70 (Ku) autoantigen protein mRNA, complete cds.	J04611
TAGACTAGCA	1514.	Human globin gene.	M69023
GTGAGCCCAT	1515.		
CTGCCGCCGA	1516.		
GGTCACATTA	1517.		
CTGGGCCTGC	1518.		
CGATTCTGGA	1519.		
ACTGGTACGT	1520.		
AAATGCCACA	1521.		
CAGGGTCCTG	1522.		
TTGTAAAATA	1523.	Homo sapiens HUMFLI-1 mRNA.	X67001 S44
GACCCACTAC	1524.	Human lymphocyte activation antigen 4F2 large subunit mRNA.	J03569
TCAATAAAGA	1525.	Homo sapiens QRSHs mRNA for glutaminyl-tRNA synthetase.	X76013
GGGAGCTGCG	1526.		
GTGTAATAAG	1527.	Human hnRNP A2 protein mRNA.	M29065
CCTTCCCTGA	1528.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TTCACAGTGC	1529.		
CTGGAGGCAC	1530.		
GACTTTGGGA	1531.	Homo sapiens mRNA for neuropathy target esterase.	AJ004832
CGGGCCGTGC	1532.	Homo sapiens mRNA for Glyoxalase II.	X90999
TCACCTTAGG	1533.		
ACTGGCGAAG	1534.	Human hLON ATP-dependent protease mRNA, nuclear gene encoding	U02389
CAGTTACTTA	1535.	Homo sapiens mRNA for HS1 protein.	X57346
CCAAGAAAGA	1536.	Homo sapiens polyadenylate binding protein mRNA, complete cds.	U75686
CCTGCAATCC	1537.		
CCTGAGCCCG	1538.		
GGAACAGGGG	1539.		
GGCCAGCCCT	1540.	Human liver-type 1-phosphofructokinase (PFKL) mRNA, complete cds.	X15573
TCTGCCTGGA	1541.		
TTTGTTCATT	1542.	Homo sapiens HnRNP F protein mRNA, complete cds.	L28010
TGCCTGTAGT	1543.	Hum ORF (CEI5) mRNA, 3' flank.	M80651
CACCTGCAAT	1544.		
CACTACACGG	1545.	Human rapamycin-binding protein (FKBp-13) mRNA, complete cds.	M65128
GGGCAGCTGG	1546.		
CAAGGATAAG	1547.		
GTGCCTAGGG	1548.		
GCAGGCTGTG	1549.	Human prolidase (imidodipeptidase) mRNA, complete cds.	J04605
TACATCCGAA	1550.		
GTATGGGCCC	1551.	Human glycoprotein mRNA, complete cds.	M80927
CTGAGGTGAT	1552.		
GAGGTCCTTC	1553.		
TCCTGCTGCC	1554.		
CATCTGTGAG	1555.	Homo sapiens DAP-1 mRNA.	X76105
CCTGTGGTTT	1556.	Human protein p78 mRNA, complete cds.	M80359
ATGATCCGGA	1557.	Homo sapiens calcium-ATPase (HK1) mRNA, complete cds.	M23114 J04
AGGAGTCGAC	1558.	Human ubiquitin fusion-degradation protein (UFD1L) mRNA, complete	U64444
TGTCCGTCAC	1559.		
GGCGTCCTGG	1560.		
CACTTGCCCT	1561.	branchio-oto-renal syndrome candidate gene {3' region} [human,	S82655

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TGTTCCACTC	1562.	Homo sapiens CD39L2 (CD39L2) mRNA, complete cds.	AF039916
TGTGTTAAAA	1563.		
AGTGCACGTG	1564.		
CAAAACTGGC	1565.		
TCTTCATACC	1566.		
GGTAGCCTGG	1567.	Human xeroderma pigmentosum group E UV-damaged DNA binding factor	U32986
GAGTTATGTT	1568.		
TGGAAATAAA	1569.		
CTTCTGGGGA	1570..	Homo sapiens rhoG mRNA for GTPase.	X61587 S38
TTTGATGTAT	1571.	Human messenger RNA fragment for the beta-2 microglobulin.	V00567 J00
TTAATAAATG	1572.	Homo sapiens Cre binding protein-like 2 mRNA, complete cds.	AF039081
TGAGCCACCG	1573.		
GTTGGGGTTA	1574.		
GCCATTATAA	1575.	Homo sapiens mRNA for lysosome-associated membrane protein-2.	X77196
CCCTGGGTTT	1576.		
CTAATAAATG	1577.		
CTGCTATGTG	1578.	Human ras-like protein mRNA, complete cds, clone TC10.	M31470
TTTCATCGTA	1579.		
AACGTGCAGG	1580.	Human mRNA for argininosuccinate synthetase.	X01630
AGCTGTTCAA	1581.		
CCTTGGCCTC	1582.		
GACAGTGTGG	1583.	Homo sapiens mRNA for NuMA protein.	Z11583
CTGGCAATGA	1584.		
CTCAAGCACC	1585.		
CTGGGACTGA	1586.		
GATTGTGCAA	1587.	Human mRNA for KIAA0183 gene, partial cds.	D80005
GTGGCTCATA	1588.		
GTTGCTGCCC	1589.		
TGAATGTCAA	1590.		
TGACGTCAGC	1591.		
TGGTTTGCGT	1592.		
TTGATTTCCT	1593.	Homo sapiens ICERE-1 mRNA, complete cds.	AF007790
GCAACGTCAG	1594.		
CCTTTGAACA	1595.		
TTTTATGGAA	1596.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
GTCCTTTCTG	1597.	Human heparin-binding EGF-like growth factor mRNA, complete cds.	M60278
TGGAGAGCAA	1598.		
GGGAATGTGG	1599.		
CCTACAGGGT	1600.		
CTGATTTATT	1601.		
CTGGGTAGCA	1602.	Human cGMP phosphodiesterase gamma-subunit (PDEG) mRNA, complete	M36476
CCCCTTTAAC	1603.		
CCCGAAACCA	1604.		
TCTTCTCCCT	1605.	Human mRNA for hepatoma-derived growth factor, complete cds.	D16431
TGGTTTTTGA	1606.		
CACCATTCAG	1607.		
CTTTTCAGCA	1608.		
CAGGCCTCTG	1609.		
CAGTCAGGCT	1610.		
CCAACCCATC	1611.		
ATGACCTGAA	1612.		
TGGATGGCTT	1613.		
GTTGGGGGTA	1614.	Homo sapiens mRNA for transcription factor AP-4.	X57435
CAAATAAAAA	1615.	Homo sapiens (clone CD18) tumor necrosis factor receptor 2 related	L04270
TCCATAAGGA	1616.		
CAAAGACAAT	1617.		
TCTTTCCCCA	1618.		
TCTTTGGCCT	1619.		
TGATTGGCTT	1620.	Human alpha-N-acetylgalactosaminidase mRNA, complete cds.	M38083
TGCAGAACGG	1621.		
TGCATCAATA	1622.		
GCAGCGCCTG	1623.		
TGCTAAAAAA	1624.		
GTGTCTCCCG	1625.		
CCCTACCTTC	1626.		
TACCACCTCC	1627.	Human pregnancy-specific beta-1-glycoprotein mRNA, complete cds.	M17908 J03
AGCACCTCCG	1628.		
CTGTGCTCGG	1629.	Human mRNA for mitochondrial short-chain enoyl-CoA hydratase,	D13900
CTGTGTGACT	1630.	Human short chain acyl-CoA dehydrogenase mRNA, complete cds.	M26393
CTTAAGGATT	1631.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
CTTACAACCG	1632.		
CTTCGGATGT	1633.	Homo sapiens mRNA for SPOP.	AJ000644
CTCAAAAAAA	1634.		
ATTAAAGTGC	1635.		
AACGGGCCCT	1636.		
AAGAGTTACG	1637.		
GGAGGTGGGA	1638.		
AGATAATGTT	1639.	Human fur mRNA for furin.	X17094
TGTATTCCAC	1640.		
AGCCTGTAGT	1641.		
AGGGATCCTA	1642.		
ATATAGGTCG	1643.		
ATCACGCCAC	1644.		
ATCCAACTTA	1645.		
CAGAGACGTG	1646.	Human dystroglycan (DAG1) mRNA. complete cds.	L19711
ATGGCTGCTG	1647.	Homo sapiens mRNA for KIAA0664 protein, partial cds.	AB014564
CCAATCTCAT	1648.		
ATTACACCAC	1649.	Homo sapiens full length insert cDNA clone ZD46F04.	AF086284
AGAACCTTTC	1650.		
GAAGCCAGCC	1651.	Human 4E-binding protein 1 mRNA, complete cds.	L36055
TGGGTCTGAA	1652.		
GGCATCGTTG	1653.	Human mRNA for HLA-Cw*0702, complete cds.	D38526
GTGTGTGTGT	1654.	Homo sapiens mRNA for beta 3 adrenergic receptor.	X70811
GGCGTTGTCT	1655.		
GGGCATCTCA	1656.		
GGGCGAGAAC	1657.	Homo sapiens huntingtin interacting protein HYPL mRNA, partial cds.	AF049614
GGGGCCCCCT	1658.	Homo sapiens mRNA for NA14 protein.	Z96932
GGTGTGCTTG	1659.	Homo sapiens clone 24736 mRNA sequence.	AF055021
AACGGGGCCT	1660.		
GTGGTATGTG	1661.		
GCCAAGCCTG	1662.	Human mRNA for protein p68.	Y00097
GGATGTAGAG	1663.		
ACAAAGCCCC	1664.		
CTGGGACTGC	1665.		
CTGCGAGTGA	1666.		
CTCTTTGATT	1667.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
CCCACCAGGA	1668.		
CTAGTATAAG	1669.		
CCTTTGCACT	1670.		
CCTGTAATAC	1671.	Homo sapiens full length insert cDNA clone ZB95G04.	AF086176
GTCTTACTTT	1672.		
GAGGCACTGA	1673.	Human Ikaros/LyF-1 homolog (hIk-1) mRNA, complete cds.	U40462
TGTTCTTTGC	1674.		
TTAATATGTG	1675.		
TTGACACACG	1676.		
TTGGCCCAGA	1677.	Human IL-4-R mRNA for the interleukin 4 receptor.	X52425
TTTAATACAT	1678.		
TGCCTTGAAA	1679.	Homo sapiens COX4AL mRNA, complete cds.	AF005888
GGCCTTTTTT	1680.	Human mRNA for histone H1x, complete cds.	D64142
GACATATGTA	1681.	Homo sapiens coxVIIb mRNA for cytochrome c oxidase subunit VIIb.	Z14244
GAGGAATTGG	1682.		
GTTGATTGTA	1683.		
GAGGATTTTA	1684.	Homo sapiens ERC-55 mRNA.	X78669
CCCATCGGCC	1685.		
GAGGGTCTTG	1686.		
GATGCTAACC	1687.		
AAATGGCTTG	1688.		
TTACTAAATG	1689.		
TCAAAAAAAG	1690.	Homo sapiens partial mRNA; ID EE2-16F1.	AJ227918
GTGGATGGAC	1691.		
CATTTGTAAT	1692.	Human HepG2 3' region cDNA, clone hmd3c12.	D16914
TGTGGCCTCC	1693.		
ATGTTAGGGA	1694.	Homo sapiens vesicle soluble NSF attachment protein receptor (VTI1)	AF035824
TTCAAAGGAA	1695.	Human mRNA for KIAA0051 gene, complete cds.	D29640
GCCTTTCCCT	1696.		
CCCAGGTGTC	1697.		
CAGTATGTCC	1698.		
CATACTTTAA	1699.		
CATCCTCTCT	1700.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
CATTTATCAT	1701.	Human protein tyrosine phosphatase PTPCAAX1 (hPTPCAAX1) mRNA.	U48296
CCAAGTGAAC	1702.		
CCAATTGAAG	1703.		
CCACTGCTGC	1704.		
CAGCACCTGA	1705.		
CCATTATTTT	1706.		
CAGAAGCAAA	1707.		
CCCAAGTGCC	1708.		
CACAAACAGT	1709.		
CCCACTTGCC	1710.		
GCTGAAGATG	1711.		
CCCATAAGGA	1712.		
CCCATTCACA	1713.		
ATTCCAAGGA	1714.		
CCACTTACGA	1715.		
CACCAAAAAA	1716.		
CTCAGCAAAC	1717.		
ATTGGGACAG	1718.		
ATTGTAAATT	1719.		
CAAGACTGTT	1720.	Human cyclin A/CDK2-associated p19 (Skp1) mRNA, complete cds.	U33760
CAAGCAAAAT	1721.	Human NifU-like protein (hNifU) mRNA, partial cds.	U47101
TTAAACTTAA	1722.	Human mRNA for HM89.	D10924
CCCACCGGTG	1723.		
TGTATGTGGT	1724.		
GGATACAGGA	1725.		
TTACTGATTT	1726.		
TTACTGTGTA	1727.	Homo sapiens KIAA0410 mRNA, complete cds.	AB007870
TGTGGGTATT	1728.		
TTGAATTCAA	1729.		
TTGAGTAGGA	1730.		
TCACAATACA	1731.	Human cyclophilin-40 mRNA, complete cds.	L11667
TCCATCAAGA	1732.	Homo sapiens clone 23598 mRNA. complete cds.	AF035309
TGGGGGCACC	1733.	Homo sapiens I-Rel mRNA, complete cds.	M83221
TGGTTCTATA	1734.		
TGGTTTTGGC	1735.		
CCCGAGAAAG	1736.		
TGTAGCATCA	1737.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
CCCAACCGGT	1738.		
TCAGTTTGAA	1739.		
TTAGTTAAGC	1740.	Homo sapiens mRNA (clone p5) for archain.	X81198
TGTATTTATA	1741.		
TTGCAACCAA	1742.		
TTCTTCTTCT	1743.		
TTAGCCAGGA	1744.	Human LLGL mRNA, complete cds.	D50550
TTATACAGCC	1745.		
TGTCTTTAAA	1746.		
TTATCATAGC	1747.		
TTCTGGGGGC	1748.		
TACATATGGA	1749.	Human mRNA for KIAA0248 gene, partial cds.	D87435
CAGGCCTGGC	1750.		
TGTAGATGTA	1751.		
CCTAAAGGAG	1752.		
CGCGACGATG	1753.		
CCGTGTTAAT	1754.		
CCCTCTGTGA	1755.		
CCCTGGGTTA	1756.		
CCGAGGAAGG	1757.		
CCGATTCGTC	1758.		
CCGCCATCTC	1759.		
CCGCTTCTGC	1760.		
CCGGAATGTG	1761.		
CCTTAGTTTA	1762.		
CCGGGCACAG	1763.		
CAAGGTGCAA	1764.		
CCGTTCTGGA	1765.		
CTACCTTGGT	1766.		
CCTCCCAAGA	1767.		
CCTGACGCTC	1768.		
CCTGATGTGG	1769.	Human AHNAK nucleoprotein mRNA, 5' end.	M80902
CCTGCCAAAA	1770.	Homo sapiens mRNA for serine palmitoyltransferase, subunit II.	Y08686
ATGTGGGCTC	1771.	Homo sapiens garp gene mRNA, complete CDS.	Z24680
CCGGGACATC	1772.		
AGAGAATCAG	1773.		
AGGAGTGGTT	1774.		
AGCGCTGAAA	1775.		
AGCGCCCTGG	1776.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
AGCCCTACAG	1777.		
CCTGTAGCCC	1778.	Human fgr proto-oncogene encoded p55-c-fgr protein, complete cds.	M19722 J03
CCTTGCATTC	1779.		
CACAAATGCT	1780.		
CCCTAGGGCC	1781.		
CACCTCCCGG	1782.		
CACCTCTCCT	1783.		
CACCTGTCCT	1784.		
CACTGCCTGT	1785.		
CACTGTCTCA	1786.		
CAGAAACAGA	1787.	Homo sapiens clone 24670 mRNA sequence.	AF055019
CAGAAATATA	1788.		
CACAAACGGA	1789.		
CGTCAAGATT	1790.	Human farnesyltransferase alpha-subunit mRNA, complete cds.	L10413
GCTGGGATCA	1791.		
CCTTCTTGAT	1792.		
CTATCACTAC	1793.		
CCTTGGGCCT	1794.		
CCTTGTTTAA	1795.		
CCTTTCTGTA	1796.		
CGCCGCGGCT	1797.		
CCCCCCTTCC	1798.		
CGGTCCCATT	1799.		
CCTGGAAGGG	1800.		
CGTTTTCTTG	1801.		
CTAAAGGAGG	1802.	Homo sapiens transcription factor (HTF4A) mRNA, complete cds.	M83233
CTAACAGGAT	1803.		
CTAATTCTTT	1804.		
TTAAAACAAA	1805.		
CCTTCTGCCA	1806.		
TCTGCAAAAA	1807.		
TATATTTCCT	1808.		
TAGACATTTG	1809.		
TAGATCCTGT	1810.		
TAGGACCCTG	1811.	Homo sapiens clone 24664 PH-20 homology mRNA, complete cds.	AF070608
TAGGGAATGA	1812.		
TGGAGCACAG	1813.		
TAGTTGATGG	1814.		
CTCAGCCTGA	1815.	Human HepG2 3' region MboI cDNA.	D17172

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
		clone hmd2f10m3.	
CAGGTGTCTT	1816.	Homo sapiens mRNA for PkB kinase.	Y15056
CACGCGCTCA	1817.	Human mRNA for RPB5 (XAP4), complete cds.	D38251
TATAGCTACC	1818.		
TCTGCAGGTC	1819.		
TACTGTATGT	1820.		
GTCAGGCCTC	1821.		
TTTAGACTTT	1822.	Homo sapiens MAD-related gene SMAD7 (SMAD7) mRNA, complete cds.	AF010193
TGCCAATAAC	1823.		
TGCAGGGCCT	1824.		
TGCAGGCTGG	1825.		
TGATGGCTCC	1826.	Homo sapiens arylsulphatase A mRNA, complete cds.	X52151 J04
TGATGCACCT	1827.		
TGAGATTGAG	1828.		
TGAAACAAGC	1829.		
TCTTGGCATA	1830.		
TCTTGATGTC	1831.	Homo sapiens full length insert cDNA clone ZC48G12.	AF086210
TTAAGAGGGG	1832.	Homo sapiens histone-binding protein mRNA, complete cds.	M97856
TATATTGCAA	1833.		
TAGAAAAATA	1834.	Homo sapiens RNA for neuroleukin gene.	X16539
TAGTGCACAT	1835.		
TATGTTGGGG	1836.		
TATGCGTTTG	1837.	Homo sapiens full length insert cDNA clone YW23E08.	AF086023
ACTTGCGAAT	1838.		
TATTAGATGT	1839.	Human CC chemokine STCP-1 mRNA, complete cds.	U83239
TGGTTACAAA	1840.	Homo sapiens clone 23596 mRNA sequence.	AF038203
TATTTATCCA	1841.	Human mRNA for leukocyte-associated molecule-1 alpha subunit (LFA-1	Y00796
TATTTTGGAG	1842.		
TCAACAGCAG	1843.		
TCAAGAATCC	1844.		
TCACAGTGCC	1845.		
TACTTAATTG	1846.		
TATGCCCTAT	1847.		
GCTTTTCAGA	1848.	Human VEGF related factor isoform VRF186 precursor (VRF) mRNA.	U43368

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TTGCTTCTTA	1849.		
TTGGGGTTTA	1850.		
TTGGGTTTTC	1851.	Homo sapiens can mRNA.	X64228 S89
TTGTGAAGGA	1852.		
TTGTGGAAAG	1853.		
TTTAAAACTT	1854.		
TACCACAGCC	1855.		
TACCAGAGTC	1856.	Homo sapiens mRNA for serotonin receptor.	Z36748
TACCAGCCAG	1857.		
TACCCAGGGC	1858.		
TACCTTTTCC	1859.		
TTTCTGCTAA	1860.	Homo sapiens mitochondrial HSP75 mRNA. complete cds.	L15189
TCACATTCCT	1861.		
TGCTCTTTCC	1862.		
TGGGTGACCA	1863.		
TGGGTTAATA	1864.		
TGGTCCCCCT	1865.	Human mRNA for KIAA0028 gene. partial cds.	D21851
TGGTGACAGC	1866.		
TTTTATGGGT	1867.	Human HepG2 3' region cDNA, clone hmd4a12.	D16930
TTTGTGGCTA	1868.		
TCACTCCTGG	1869.		
TGGAGCGCTA	1870.		
TGTGGTGTAG	1871.	Human (clone pA3) protein disulfide isomerase related protein	J05016
TGCCCGGCAG	1872.		
TGCCCTGGTT	1873.		
TGCTTTCAAA	1874.		
TGCGTGGCTA	1875.		
TGGGCCAGCC	1876.		
TGCTGATAAG	1877.		
TGCTGTGAAA	1878.		
TGTGAAGATT	1879.		
TGTGCCACTA	1880.		
TGCCATCAAT	1881.		
TTGATTTCTG	1882.		
TGCTGGGTAC	1883.		
TGTGAGCCCT	1884.		
TGTGTTCCTG	1885.		
TGTTCCAGAT	1886.	Human syntaxin 3 mRNA. complete cds.	U32315
TGTTTCCTTA	1887.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
TGCGGGCCTG	1888.		
TCAGAACAGT	1889.	Human G-rich sequence factor-1 (GRSF-1) mRNA, complete cds.	U07231
TCTAGCTGGA	1890.		
TCTAAAGAGT	1891.		
TCGGGTTTAC	1892.		
TCGGGTCCCT	1893.		
TCGGAGCCCC	1894.		
TCCCATCATA	1895.		
TCCAGCTCTG	1896.		
TCCAATACTG	1897.	Human dynamitin mRNA, complete cds.	U50733
TCATCTTCAA	1898.	Human autoantigen calreticulin mRNA, complete cds.	M84739
TCATCTCCCT	1899.		
TCTGGCTGGG	1900.		
TCAGTGGTAG	1901.		
TCACTGGGGA	1902.		
TGGGCTCCTC	1903.		
TCAGAAGTTT	1904.		
TCAGACGCGG	1905.		
TCAGGCTGTT	1906.	Homo sapiens mRNA for beta-centractin (PC3).	X82207
TCAGTGCGCA	1907.		
TGCTGTGGGG	1908.		
TGCTTGCAAC	1909.	Homo sapiens short form transcription factor C-MAF (c-maf) mRNA,	AF055376
TTGCTAAAGG	1910.		
TGGACTGGTA	1911.		
TTTCATTGCC	1912.	Homo sapiens full length insert cDNA YN99C01.	AF075051
TGGATATGAA	1913.		
TTTCTCTAAG	1914.		
AGAGTAACTG	1915.		
TGGATTGCCA	1916.		
GAGCCCCTTG	1917.		
GTGGTGTGCC	1918.		
GTGTGGGAGA	1919.		
GTGTTACCCA	1920.		
GTGTTCTGTG	1921.		
GTTAACTGGG	1922.	Homo sapiens mRNA for putative RNA helicase, 3' end.	AJ223948
GGAGGCTGGA	1923.	Human cell adhesion molecule L1 (L1CAM) mRNA, complete cds.	M74387
GTGGCACGCG	1924.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
GATGGCAGGG	1925.		
GCACAAAGGG	1926.		
GACACACAGA	1927.		
GACCACACAC	1928.		
GGCAGCCAGG	1929.		
GAGCAGGAGC	1930.	Homo sapiens mRNA for KIAA0600 protein, partial cds.	AB011172
GTGGCTCGTG	1931.	Homo sapiens (xs130) mRNA, 260bp.	Z36786
GAGGATCTGC	1932.		
GAGGCAAGAC	1933.		
GAATACGCAC	1934.		
GATAGAGGGA	1935.		
GAACTCAGGC	1936.	Human HCF1 gene related mRNA sequence.	L20010
GCAAATATAT	1937.		
GCAAATCTGA	1938.		
GCAACGGCCC	1939.		
GCAACTGCAC	1940.		
GCAAGAAGAA	1941.		
AGATTTGGAA	1942.		
GACTCAGGGA	1943.		
TACACCAAGA	1944.		
GTTGTGGCTA	1945.		
GTTGTGGTAC	1946.		
GTTTGCCTGA	1947.		
TAAAAGGATG	1948.		
TAAAGCAGTA	1949.	Homo sapiens mRNA for restin.	X64838 S38
GTGAGCAAGA	1950.	Human mRNA for a presumptive KDEL receptor.	X55885
TAAGAAGCTT	1951.		
GTTATATCCA	1952.		
TAATCACCAG	1953.		
TAATGAACTA	1954.	Homo sapiens mRNA for KIAA0639 protein, partial cds.	AB014539
TAATGGGAGT	1955.		
GTGGTGTGCA	1956.	Homo sapiens RNA transcript from U17 small nucleolar RNA host gene.	AJ006835
TAATTTTGAA	1957.		
GTTCACATTT	1958.		
TACAGAGCCC	1959.		
TAAAGTGTCT	1960.		
GTGGTGGGCG	1961.		
GTGATGTACG	1962.		

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
GTGATTTTAC	1963.	Homo sapiens putative protein kinase regulator mRNA, complete cds.	AF062077
GTGCCCAGTC	1964.	Homo sapiens mRNA for KIAA0633 protein, partial cds.	AB014533
GTGCCCTTGA	1965.		
GTGCGCTGAC	1966.	Human MHC class I HLA-Cw1 gene, complete cds.	M26429
GTGCTAAGCG	1967.	Human mRNA for collagen VI alpha-2 C-terminal globular domain.	X15882
GTGCTGGCAG	1968.		
GTTCTGCCTC	1969.		
GAGTACCCCT	1970.		
TAATGGTAGC	1971.		
GCAGAAAGTT	1972.	Homo sapiens diphthamide biosynthesis protein-2 (DPH2) mRNA,	AF053003
GCTGTAGGGG	1973.		
GCGAAACCTT	1974.		
GCTTATGTTA	1975.		
GCTTCCTAAG	1976.		
GCTTCTGAAC	1977.		
GGAAGGCAAG	1978.		
GGAAGGTGGA	1979.		
GGAAGTTTCG	1980.		
TACAGCACGG	1981.	Homo sapiens microsomal glutathione S-transferase 3 (MGST3) mRNA,	AF026977
GCTGGTTCCT	1982.		
GCCTCCCCCA	1983.		
GCAAGGCAGA	1984.		
GCACTTCAAA	1985.	Homo sapiens clone 24675 mRNA sequence.	AF070585
GCTAGGTTTA	1986.		
GCAGAGCAGT	1987.	Human LYL-1 protein mRNA, compiete cds.	M22637
GCAGGACCCT	1988.		
GCATTTAGTT	1989.		
GCCAAACTTG	1990.		
GCGAGCTGGC	1991.		
GCCGGCCGGA	1992.		
GCGACCAACA	1993.		
GCCTGCTTGG	1994.		
GCCTGTTGGG	1995.		
GCCTGTTTGG	1996.	Human bilirubin UDP-glucuronosyltransferase isozyme 1 mRNA,	M57899

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
GCGAAACCGC	1997.		
GCACGCGTAA	1998.		
CTGTTTGTCA	1999.		
CTGGCCTGTA	2000.		
CTCATAGGGA	2001.		
CTCCTACCTG	2002.		
CTCTCATCTC	2003.		
CTCTCTGTGG	2004.		
CTCTTCAGGA	2005.	Homo sapiens phosphomevalonate kinase mRNA, complete cds.	L77213
CTGAGTTAGG	2006.		
CTGCCCCACA	2007.	Homo sapiens nuclear protein Skip mRNA, complete cds.	U51432
GACAAAGCAA	2008.		
CTGGCCGACT	2009.	Homo sapiens p160 mRNA, partial cds.	U88153
GCACAGAGCC	2010.		
GCAATTCACC	2011.		
CTGTGCCAAT	2012.		
GCTGATCTGT	2013.		
CTTATGTATT	2014.		
CTTCTTTCCA	2015.		
CTTTTCAAGA	2016.	Homo sapiens, gene for Membrane cofactor protein.	X59405
GAAAGATTGC	2017.		
CTGCCCTGGG	2018.		
GCTGTGGTCC	2019.	Human HepG2 3' region cDNA, clone hmd3d10.	D16918
GCGATGGGGG	2020.		
GCGCACCGCT	2021.		
GCGGAAACTG	2022.		
GCGGCCACCA	2023.		
GCGTGCTCTC	2024.		
TAAGTCTATA	2025.	Homo sapiens RNA for Fc receptor, PC23.	X62572 Y00
CTGGGATCAT	2026.		
AAGGCAAAGA	2027.		
AGGGCTTTCC	2028.		
ACCTACAACG	2029.		
AGTTCTATGG	2030.	Homo sapiens clone 23728 mRNA sequence.	AF038199
AAAATAAACA	2031.		
AAGATCCTCA	2032.		
AAGAGCTAAT	2033.	Human mRNA fragment for glutaminyl-tRNA synthetase (EC 6.1.1.18).	X07466

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
AAGAAACTAA	2034.	Homo sapiens mRNA for telomeric DNA binding protein (orf1).	X93511
AACGTTCTTG	2035.		
AACATTGGCT	2036.		
AACAGCTTTA	2037.		
AACAATTGGG	2038.	Homo sapiens EWS/CHOP chimeric fragment.	X92120
GTTGGTCCTC	2039.		
AAACTCGAGC	2040.		
AGTAAACTGA	2041.		
ATCTTTTCTC	2042.	Human eosinophil Charcot-Leyden crystal (CLC) protein	L01664
ATGACTGTGC	2043.		
ATGATACCTG	2044.		
ATGATTTCAG	2045.		
ATGGACCCCG	2046.		
ATGGCACCAT	2047.		
ATGGTGTATG	2048.		
AACAACTGGC	2049.	NAT=CpG island-associated gene [human, mRNA, 1741 nt].	S78771
AATGTAATCA	2050.	Human sorcin (SRI) mRNA, complete cds.	L12387
CTCAGTGGAA	2051.		
ACCGTATTCC	2052.		
ACTGCTCATT	2053.		
ATCCCACTGA	2054.		
GCCAGCTGTG	2055.		
ATTCCTAGGG	2056.		
AGAGCAAAAA	2057.		
AGGCTTCTCA	2058.	Human sialophorin (CD43) mRNA, complete cds.	J04536
AGACCACAAC	2059.		
AGAATGCTGA	2060.	Human myeloid progenitor inhibitory factor-1 MPIF-1 mRNA, complete	U85767
AGAAGCTGTG	2061.		
AGAAAAAAAC	2062.		
ACTTCTGGAA	2063.		
ACTTAGGCTT	2064.		
ACTGTGCCAC	2065.		
AGGTACGGAA	2066.		
AGTGCCGTGT	2067.	Human interferon-induced cellular resistance mediator protein (MxA)	M30817
AGGTTTTCTA	2068.	Homo sapiens embryonic ectoderm development protein mRNA, partial	AF070418

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
ATCCATCTGG	2069.		
ATCATTACTA	2070.		
ATATACTGTA	2071.		
ATAGGATACT	2072.		
ATAAGGTACA	2073.		
AGTTGTCCCG	2074.	Homo sapiens clone 24561 unknown mRNA, partial cds.	AF055010
AGGCCACCTC	2075.		
AGTGTCCCGG	2076.		
AGGCGGAGGT	2077.		
AGTAGTCTGC	2078.		
AGTACCTGTC	2079.		
ACCAACACAC	2080.		
AGAGGGTGGG	2081.		
GGGACGAGAA	2082.		
ACCGGCGTGG	2083.		
GTCGTTGGTG	2084.		
GTCTTAACTC	2085.	Homo sapiens Dim1p homolog (hdim1+) mRNA, complete cds.	AF023611
GTGACGCCCC	2086.	Homo sapiens full length insert cDNA clone ZD76G10.	AF086408
CTCAACAATG	2087.		
GTAGATGATG	2088.		
GGGCCGCTCA	2089.	Homo sapiens mRNA for KIAA0602 protein, partial cds.	AB011174
GGCAGCTGGA	2090.		
GGCAGGCCTG	2091.		
GGCAGTGACT	2092.		
GGCCCACACC	2093.		
GTCCCTCAGC	2094.		
GGGAAATCCC	2095.		
GTCCCACGGG	2096.		
GGTCTTCTCT	2097.		
GGGCCCCCAA	2098.		
GTGATGGGGA	2099.		
GGGCTCTGAG	2100.		
GGGGAGTAGG	2101.		
GGGGCAAGTG	2102.		
GGGGCTGTGG	2103.	Human TFIIIC Box B-binding subunit mRNA, complete cds.	U02619
GGGGGAAAAT	2104.		
GGGTGTCACT	2105.		
GGTAGGGGTT	2106.	Homo sapiens ubiquitin conjugating enzyme 12 (UBC12) mRNA, complete	AF075599

TAG	SEQ ID NO	DESCRIPTION	ACCESSION
GGGCATTTCT	2107.		
AGATCTGGGA	2108.		
GGCCCATATG	2109.		
ACAGGAAACT	2110.		
GTTGAGAGAG	2111.		
ACATTTCAAC	2112.		
ACATTGGTAA	2113.		
AAGATGCACA	2114.	Human mRNA for phosphodiesterase I alpha, complete cds.	D45421
ACAAGACGGC	2115.		
AAGGAGTTCC	2116.		
AATGGGAGTT	2117.		
AATGCTTGAT	2118.	Homo sapiens IEF 7442 mRNA.	X72841
AATGCCCCAC	2119.		
AATCAAGGTG	2120.		
AATAAAGCAA	2121.		
GTCCTCAAGC	2122.		
ACTGCCCCAA	2123.	Homo sapiens full length insert cDNA clone ZD38B07.	AF086245
ACCCGCCGGC	2124.		
GTCATACACC	2125.		
GTGAGGGGTG	2126.		
GGTGACTTCA	2127.	Human DNase1-Like III protein (DNAS1L3) mRNA, complete cds.	U56814
GGTGCTTATG	2128.		
GGTGTCTCGC	2129.		
GGTTAATTGA	2130.		
GGTTCCTGGC	2131.		
GGTTGGGGTA	2132.		
GGTTGGTGGT	2133.		
GGTCATTGTA	2134.		
GTATAATAGC	2135.	Human mRNA for U2 snRNP-specific A' protein.	X13482
GGTCAGTCTC	2136.		
AAGGTGCATA	2137.	Human Kox15 mRNA for zinc finger protein, partial.	X52346